VOLUME 55 • NUMBER 12 • DECEMBER, 1959

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Subscriptions: $3 per year for members; $6 for nonmembers; $7 for foreign. Single copy: 75 cents.

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Rebirth of a Specialty

Twenty-five years ago it was still acceptable for a physician to drop out of general practice for 18 months and then reestablish himself as a specialist in eye, ear, nose, and throat. Of course, this amount of training was inadequate, but for the knowledge of the specialty of that period, he could do acceptable work in his field. In the passing interval the branches of otolaryngology and ophthalmology have established separate and individual boards, and board requirements for otolaryngology are now 4 years including 1 year of general surgery.

This dynamic development occurred during the time the rest of the profession was convinced that the specialty was doomed by antibiotics and chemotherapy. The wonder drugs expanded the horizon of the branches of medicine and particularly otolaryngology. Better tools have been developed for anesthesia as well as ready supply of blood replacement. Gone were otitic meningitis, brain abscesses, and osteomyelitis of the frontal bone, but quickly taking their place were pharyngectomies, wide field laryngectomies, and neck dissection for cancer of the head and neck which previously had been doomed to palliation with irradiation therapy. Described in this *Journal* recently by Dr. W. P. Anthony,* reconstructive middle ear surgery has provided hearing improvements in conditions previously considered irreversible. The boy who had no ear drum now has good serviceable hearing and can participate in water sports since he has had his drum replaced by a tympanoplasty. The young woman with otosclerosis will not have a therapeutic abortion be-

*Anthony, W. P.: Renaissance in Otology, Texas J. Med. 55:255-257 (April) 1959.

cause her stapes may now be mobilized and hearing again restored to normal. With development of the surgical approach to rhinologic problems on an enlightened basis, reconstruction of the external nasal pyramid has added to the correction of nasal obstruction due to trauma with cosmetic improvement as an added dividend. The specialty is even tending to subspecialize into otology, rhinology, and laryngology according to the preferences of the individual since it is difficult to be equally adept at rehabilitation of the deaf and at radical head and neck surgery.

In the meantime the trend in undergraduate teaching has deemphasized the surgical specialties to the point where the student may actually have only 6 hours of lectures to cover the extensive field of otolaryngology. In the winter months the patient load of the general practitioner and the pediatrician may be as high as 50 per cent for upper respiratory complaints. They must rely on the erroneous impression that a working knowledge of antibiotic therapy eliminates the necessity for special training in this field. The present day teaching in some institutions discourages or even forbids myringotomy in acute otitis media since there is no opportunity to associate an irreversible conductive deafness with past history of ear infections. The vocabulary has been reduced to the point where the word "sinus" covers all ailments of the nose and "fungus" all sore ears. Of equal importance, the otologist continues to pick up the perceptive deafness due to the indiscriminate use of ototoxic drugs such as streptomycin, dihydrostreptomycin, kanamycin, and neomycin. It is evident then that more time must be allotted to undergraduate as well as postgraduate teaching.

The predictable effect of the prophecies of doom was the swing of the pendulum to the extreme negative side for the younger men entering the specialty, but the swing back has been noticeable for the past 2 years. Trainees are not motivated by prospects of a life of ease but by the desire to occupy an important niche in the practice of medicine. The demand for otolaryngologists in all parts of the country far exceeds the supply. Income guarantees in some instances are fantastic. The young man may hang his shingle almost anywhere and soon have more work than his time permits.

—CLAUDE D. WINBORN, M.D., Chairman,
Division of Otolaryngology,
University of Texas
Southwestern Medical School, Dallas.

New Dues, Better Service

Checks to cover dues for the Texas Medical Association for 1960 will bear a new set of figures from what has been customary for a decade. It will save confusion and delay if each physician will keep in mind that state dues as of January 1, 1960, total $45 instead of $50. Dues for emeritus, honorary, inactive, resident, intern, and military memberships remain the same as before.

In 1948, existing dues of $35 per year were increased $15 to take care of payments on a new headquarters building. The mortgage agreement called for payments on the building to run to July, 1962. However, it has been possible to complete such payments in 1959. According to the provisions of the By-Law amendment adopted in 1948, the $15 building fund assessment was to be withdrawn when the building was clear of debt. In calling attention to the anticipated end to building payments, the Board of Trustees in April, 1959, reminded that taxes on the building amount to $14,700 per year, maintenance and operating costs to $15,000; that occasional remodeling is necessary to bring the building facilities in line with growing and changing services; and that the margin in operating funds in 1958 was only $2,800 with a number of meritorious requests from Association committees having to be denied because of lack of adequate funds to permit additional projects. As a consequence, the House of Delegates voted amendments providing for an end to the $15 building fund assess-

ment effective January 1, 1960, but for an increase in basic dues from $35 to $45.

Texas Medical Association dues are in the middle range among state medical societies according to surveys reported by *Medical Economics* and elsewhere. State dues range from a high of $140 in Utah and $100 in Nevada to $7 in Maryland and $25 in Ohio, South Carolina, Tennessee, Virginia, West Virginia, and Wyoming. Twenty-one state medical societies are known to have increased their dues in the past 3 years, and Texas is the only state known to have reduced total dues in recent years.

Where does the money go? The Board of Trustees, in explaining the financial status of the Texas Medical Association to the House of Delegates last spring, named the *Texas State Journal of Medicine,* the Memorial Library, and the annual session as the three services heading the list of expenditures from operating funds. The *Journal* now costs approximately $100,000 annually. Printing and mailing costs alone run about $67,000, whereas in 1948 they totalled only $32,000. The Library, which has had a sixfold increase in reference requests from physicians during the past 10 years, receives about $38,000 in the annual budget. The annual session, which cost the Association a net of only $11,700 in 1954, now costs about $30,000—but it attracts a larger attendance. Other big expenditures which the Trustees considered worth the money are the field program which brings state officials and staff members to the county societies for an exchange of views and information (a $20,000 annual expense) and the Woman's Auxiliary (supported by about $18,000 from Association funds each year).

The expanding program of services of the Texas Medical Association in recent years has been made possible without a dues increase, the Trustees said, because *Journal* advertising revenue has doubled in 5 years, income from rental of annual session exhibit space has doubled, membership has increased steadily and thus added to income from dues, and economy in management has been exercised. It was noted, however, that one-third of operating expenses have come from sources other than dues.

Texas physicians have an active, up-to-date organization which attempts to keep abreast of new needs and new techniques while not discarding or minimizing tried and true projects and methods. Informal observation of the operation of state medical societies elsewhere suggests that the Texas Medical Association is no laggard in its field and that members get value received for their dues.

The Trustees report financial affairs of the Association to be in sound condition. By freeing some of the building funds for other expenses, an even better program in the immediate future can be anticipated.

Action on the Way

The first issue of *Texas Medical Association Action,* a four page newsletter emphasizing current items of special interest to members of the Association, will be mailed to the entire membership by January 1.

Authorized by the Board of Trustees and approved by the House of Delegates for a year's trial, *TMA Action* will be issued three or four times during the year when information needs to be provided rapidly and in readily assimilable form. It will supplement the *Texas State Journal of Medicine* and substitute in some measure for the numerous individual special mailings which have been used in the past to disseminate material on Association conferences, legislation of interest, and committee projects.

In a study conducted by the Medical Society Executives Association respondents favored the newsletter as the medium of communication most effective in reaching organization members.

The new newsletter will add a personal, informal, comparatively inexpensive method of communication to the mediums already in use

to help keep Texas physicians informed. Effective methods already in use include three meetings annually (annual session, conference for county society officials, and conference on public relations), orientation program for new and transfer members, a visitation program (talks before county societies), brochures and pamphlets, exhibits (five exhibits are now available on Association services and projects), special letters of welcome to new members, and the *Journal*.

Despite repeated and various efforts to insure a well informed, active membership, some physicians remain almost totally unaware of the Texas Medical Association's programs and services. Others, though perhaps fairly well informed, are inclined to lose interest and forget their share in the organization if they are not reminded.

It is hoped that *TMA Action* will prove a welcome addition on the doctor's desk. Comments and suggestions about it will be welcome.

★ Current Editorial Comment

Texas Physicians and Traffic Accidents

In the past 10 years our population has increased steadily, and so has the volume of automobile traffic on our highways. Yet the number of deaths from traffic accidents has remained fairly constant from year to year.

This suggests that society has developed some resistance to traffic hazards and that we may see even more resistance, if we try harder. Try harder we must, as still nearly 40,000 people die yearly in this country from automobile accidents, many more than die from any of the major infectious diseases. Furthermore, except for the very few accidents due to massive coronary occlusion, brain hemorrhage, a major structural breakdown in the car, a landslide, or an earthquake, *all traffic accidents are preventable.*

Physicians have always been active in public health education and legislation. The doctors of this country realize they should use their skill, judgment, and prestige in the fight for traffic safety. The immediate past president of the Texas Medical Association, Dr. Howard O. Smith, initiated a Committee on Transportation Safety to do such work in Texas.

When we think about doctors and traffic accidents, we think first of the immediate care of the injured. We can care for them expertly only if we keep learning and relearning about the medical and surgical aspects of trauma. Therefore, postgraduate education will be an important part of this committee's work.

We should review the ambulance facilities in our cities. We should make sure that ambulance drivers are trained in first aid and that the emergency services in our hospitals are adequate. This means more than the physical layout of the emergency room. Rural hospitals without residents or interns must have a physician available always. They need a staff-sponsored emergency call system. Failure to get a doctor quickly for an accident victim sometimes will harm the patient; it always will damage the standing of the medical profession in the eyes of the public.

To make sure an accident victim can get a doctor quickly is not enough. We must be ready to cope with accidents with many casualties. They are not rare in rural areas where workers travel to and from the fields by the truckload.

The care of the acutely injured is the surgeon's job; accident prevention lies largely in the field of medicine. Endocrinological, neurological, cardiovascular, neuropsychiatric, ophthalmological, orthopedic, and other disorders may make it unsafe for a patient to drive, either permanently or temporarily. Some diseases can be controlled so well that a patient may drive while under treatment. Many drugs interfere with safe driving. Recent papers cover the medical aspects of traffic accident prevention well, and all doctors should read them carefully and retain them for reference.[1, 2] Most patients will obey if their physician tells them not to drive, or to drive only under certain conditions. A restriction of driving cuts deeply into a person's life, however, and many a patient will be so unhappy about it that his emotions will warp his judgment; he will "know better" than his doctor and he will drive, against medical advice.

When officers of the Drivers License Division think that a person cannot drive safely because of a physical or mental impairment, they turn to a physician. Often the doctor may fear that he will hurt his relationship with the patient if he instructs the officers not to give him a license. He might want to leave

Guest editorials and current editorial comments are solicited from members of the Texas Medical Association and others closely related to the medical profession of Texas. Topics should be of general interest and may pertain to scientific, organizational, socioeconomic, or philosophical subjects in the medical and health field. Manuscripts should be from 300 to 750 words in length.

this decision to a colleague less close to the patient, and in areas where this occurs often, county medical societies might appoint a board of qualified physicians to take this responsibility from the shoulders of the family physician.

All other traffic safety work falls under four headings: *enactment, enforcement, education,* and *engineering.* Not one of these is a purely medical problem, yet we have an interest in all of them.

Many people have worked for years to increase traffic safety. In Texas, the Texas Safety Association, cooperating with state and other public agencies, has led the fight. We doctors will do well to join hands with those who have worked in this field for a long time.

The following are some of the areas where we need new laws.

1. *Driving while under the influence of alcohol* is one of the most important causes of accidents. Heavy fines will deter people from driving while intoxicated. In order to fine, the courts need evidence, and a crucial piece of evidence is the alcohol contents of the blood. We need a law establishing the legal standing of blood alcohol determinations, and we need a law stating that anyone who accepts a license automatically agrees to undergo an alcohol test any time an officer requests it and that he forfeits his license if he refuses to take the test; several states already have such an "implied consent law."

2. We need better *drivers' licensing laws.* Under the present law applicants for a driver's license are examined only the first time they apply; thereafter, licenses are renewed every 2 years without examination. Only persons who have accumulated violations and persons reported for verifiable incapacitation have to undergo another examination. Most people licensed before 1940 never underwent an examination, and they, too, get a new license every 2 years, without examination. Visual acuity deteriorates with age; so do alertness, judgment, and other mental and physical prerequisites for safe driving. Age brings degenerative changes which predispose to sudden illness. Thus, drivers' licensing would be a much more effective safety measure than it is now if drivers, especially the elderly, were reexamined at regular intervals. If the examiner finds serious deficiencies, he should withhold the license and ask that a physician evaluate the applicant.

3. We need *traffic courts especially equipped to handle traffic cases* speedily and fairly, staffed by judges with legal training. At the present time, minor violations are handled by justices of the peace and by corporation court judges, many of whom have no legal training.

4. Often we cannot tell from examination results alone whether we can trust a person to do a responsible job safely and well. We need proof of formal training to evaluate his capabilities. The most practical way to make sure our young people receive formal drivers' education is to teach driving in school. We need *universal tax-supported drivers' education in all public schools.*

Why do we have to fight for these steps? Because people resent regulation; they dislike courts and fines, and they refuse to see that stricter laws would benefit them; also, because all of this will cost money, and nobody enjoys paying taxes. Yet, there is no price for lives and suffering. We must take these steps if we want to reduce the danger of travelling in automobiles.

"Engineering" applies to highways and to automobiles. We have, by and large, better highways in Texas than in most other states.

Until Congress makes laws to make cars safer we will have to rely on the buying public to demand new safety features. There is overwhelming evidence that many, many injuries due to automobile crashes could be mitigated were cars designed for greater safety. They should have seat belts, padded dashboards, safety locks on doors, energy absorbing front ends, and safety steering wheels. Of all these features, one stands out, because everybody can equip his car with it easily and at little cost, and that is the *seat belt.* Its general use would greatly reduce the death rate on the highway and the severity of nonfatal injuries. Nothing will convince the public but constant reiteration: Equip your cars with seat belts for all occupants, and train yourself and your passengers to use them always.

People have come to accept traffic injuries and deaths as an inevitable by-product of modern living. We must fight this attitude and take action so that some will live who now are doomed to die on the road.

I thank the members of the Committee on Transportation Safety of Texas Medical Association who helped me prepare this article by criticisms and suggestions, and especially Col. Homer Garrison, Jr., director, Texas Department of Public Safety, for numerous valuable criticisms.

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—Heinrich Lamm, M.D., Harlingen,
Chairman, Committee on Transportation Safety,
Texas Medical Association.

President's Page

A CHALLENGE

DR. YEAGER

December is the time to take inventory of your county medical society. Only then can each doctor be listed as a contributor or a parasite. Such an inventory can be a valuable tool if the old and new administrations will work together. Once the weak links are discovered, corrective action can be taken.

A president is enthusiastic as he starts his year. Too often, he becomes disillusioned. The fault is usually shared between the president and the society. The president is at fault when he appoints committees carelessly. Each committee chairman should be the best man for that particular job. The president should confer with the prospective chairman, explain what is expected, and learn if he is willing to do the job. Should a committee become inactive, changes should be made without thought of personal feelings. The men have been appointed to do a job for medicine, not for the president personally.

Members are at fault when attendance falls and when they adopt a "let George do it" attitude. We all have heard doctors say, "I don't want any office. Let the politicians run the society. I'll just practice medicine." That is the parasite speaking. He means that he wants others to devote their time to good society management and to good health programs while he enjoys the benefits of their good work in a completely selfish manner.

People regard the TMA in the same light as their county medical society. In your locale, you are the TMA. Criticism of medicine is actually criticism of the county society.

Our local societies have excellent leadership and able members. Much can be accomplished if the desire is present. The year 1959 has been good. Let's make 1960 even better. You have the challenge—what you do with it is strictly up to you.

F. W. Yeager, M.D.

ORIGINAL ARTICLES

The Heart in Congestive Failure

RICHARD J. BING, M.D.

Detroit, Michigan

THE DIFFERENT symposiums on congestive heart failure published in the literature have supplied the physician with a plethora of definitions for this condition. We find here minus decompensation, specific dynamic myocardial insufficiency; there are divisions of cardiac insufficiency with respect to hemodynamic and energetico-dynamic factors. In addition, the variety of clinical and experimental approaches to this problem testifies as to its complexity. Much has been written about the relation between filling pressure and ventricular work in the isolated heart. Metabolic studies have been performed on the whole organism in the hope that they may reflect on the metabolic disturbances in the myocardium. The redistribution of blood volume in cardiovascular failure and the relation of lowered oxygen tension within the heart muscle fibrils to disturbed myocardial contractility have been studied. In addition, much work has been performed in the observation of the circulatory dynamics of left and right heart failure. Out of all this has come a multiplicity of opinions which leaves only one definite conclusion: that heart failure is a protean condition with so many facets that it may well defy the establishment of a common denominator.

Congestive heart failure may be most simply defined as a disturbance in the dynamics of cardiac action leading to deficient emptying of the heart. The question arises, however, as to the causes which lead to increased residual volume of the heart, and to a relative diminution in the amount of blood expelled. One may search for an answer by studying the possible alterations in the metabolic functions of the heart muscle. Such an investigation is based on the assumption that heart failure is connected with alterations in the heart muscle, regardless of whether these are primary or follow changes in internal environment caused by disturbances elsewhere in the organism. In all likelihood, the role of the myocardium in congestive failure has many facets, just as the clinical and dynamic features of heart failure vary with the type of disorder and the mode of experimental production. However, in general, myocardial failure occurs either acutely or chronically; the former is usually observed experimentally in the heart-lung preparation, while the latter is seen in clinical congestive failure. This discussion will deal with these two types of failure and each group will be examined for evidence of disturbances in cardiac metabolism in order to clarify the role of the myocardium in the production of congestive failure.

Metabolism comprises only the chemical changes in the living cell by which energy is provided for vital processes and activities. Thus, metabolism includes only the production of energy. A discussion of the disturbances in heart muscle also should include processes of energy utilization because it is here that the changes leading to myocardial failure may be found. Disturbances in energy production may be detected by an examination of the balance of substrates across the heart muscle or by a search for defective action of individual enzymes in heart muscle. The investigation of energy utilization, on the other hand, can be carried out by a study of the contractile proteins of heart muscle. This can be accomplished on models of contractile proteins

Dr. Richard J. Bing, formerly professor of medicine at Washington University School of Medicine, St. Louis, and now professor and chairman of the Department of Medicine at Wayne State University School of Medicine, Detroit, presented this paper for the Texas Heart Association, April 19, 1959, in San Antonio.

Heart failure is a protean condition with many facets. The author discusses acute myocardial failure (especially as observed experimentally in the heart-lung preparation) and chronic failure (especially clinical) in relation to disturbances in cardiac metabolism (energy production). Also considered are disturbances in energy utilization.

From the Department of Medicine, Washington University School of Medicine and the Washington University Medical Service, Veterans Administration Hospital, St. Louis. Work supported by United States Public Health Service grant No. H-2678, American Heart Association, Life Insurance Medical Research Fund, and Tobacco Industry Research Fund.

such as actomyosin threads or bands or by a determination of the physical-chemical properties of actomyosin. Finally, the possibility must be kept in mind that the link between energy production and utilization can be broken and that as a consequence energy derived from the intermediary metabolism cannot be utilized in effective muscular contraction. Such a situation could exist if there is a diminution in the formation of high energy phosphate, or if there is defective exchange of high energy phosphate into excitational energy. An investigation of these mechanisms is difficult in a living structure because of the multiplicity of the various bonds through which energy is shunted from substrate to substrate and because the transformation of potential into mechanical energy may be understood only on the basis of quantum mechanics, which only recently has been applied in the understanding of biological energy transformation.

ACUTE MYOCARDIAL FAILURE

Acute myocardial failure can be produced experimentally in the heart-lung preparation; heart failure usually occurs spontaneously 2 to 4 hours after the heart and lungs have been separated from the rest of the organism. Many ideas have been proposed to explain this specific failure of the isolated heart, but there have been no definite conclusions. Heart failure which one sees in the isolated heart has some mechanical features in common with chronic heart failure as it occurs in patients with congestive heart failure. In both instances there is an increase in the enddiastolic pressure, dilatation of the heart, and diminution of the stroke volume. However, there are notable differences. In the first place, the element of hypertrophy is missing. Secondly, the oxygen consumption of the isolated heart is diminished, while that of the failing heart in situ remains normal. The main difference between the acutely failing heart in vitro and the heart in patients with congestive heart failure lies in the fact that in the former both cardiac work and oxygen consumption are diminished while in the latter the myocardial oxygen consumption remains normal.

What is the cause for the spontaneous heart failure occurring in the heart-lung preparation? Several possibilities exist. The first is that it is the result of alterations of the contractile proteins of the heart. Such studies have been performed on the heart muscle of individuals who succumbed to congestive heart failure and on isolated hearts with spontaneous failure. There is a diminution in the contractility of actomyosin obtained from failing human hearts; however, the contractility of actomyosin prepared from hearts failing in the heart-lung preparation remained unimpaired.

Therefore, it is likely that the mechanism of spontaneous failure cannot lie in organs of energy utlization, but must be sought in mechanisms connected with energy production. Since the utilization of substrates by the isolated failing heart remains normal, one must look for disturbances not connected with the extraction of substrates or the utilization of metabolites. A clue on the possible mechanism of spontaneous failure may be sought in the work of Rein, who showed that the inclusion of liver and spleen in the perfusion circuit of a heart-lung preparation increased myocardial efficiency. It is not clear from his studies whether the spleen actually releases a substance which is transformed by the liver into the active principle. However, it could be established here, confirming the work of others, that the inclusion of either liver or spleen increases the myocardial efficiency slightly, primarily by a diminution in the oxygen consumption of the heart. Cardiac work is not altered.

The question arose as to the nature of the active principle or principles in these organs. The likelihood existed that spontaneous myocardial failure in the heart-lung preparation results from lack of a catecholamine in either heart muscle or the perfusion fluid; the rise in myocardial efficiency resulting from the inclusion of liver and spleen in the perfusion circuit might then be the consequence of partial restoration of the depleted supply of these substances by these organs. In dealing with this problem, the question arises first, which of the catecholamines is the most likely to exert these actions? The answer lies in the relative distribution of the three likely catecholamines, dopamine, noradrenalin, and adrenalin. It is known that the spleen contains large amounts of noradrenalin because of its large supply of sympathetic nerve endings. There has never been any evidence for the assumption that noradrenalin is located outside the nervous tissue itself, nor is it likely that noradrenalin present in the nerve trunk itself is released under physiologic conditions. However, noradrenalin at the nerve endings functions as a chemical transmitter. There are considerable amounts of noradrenalin present in spleen, heart, ciliary bodies, and liver. The noradrenalin concentration in the lung is relatively low. The concentration of noradrenalin in these organs appears to be related to their adrenergic nerve supply. Direct determinations have shown that arteries and veins contain large quantities of noradrenalin. Moreover, the amounts found in various layers of the vascular wall bear a clear relationship to the vasomotor supply. Veins also contain considerable amounts of noradrenalin, illustrating the importance of veno-

motor nerves. The coronary vessels are particularly rich in noradrenalin.

In order to prove that lack of noradrenalin is responsible for the spontaneous failure of the isolated heart, and that addition of this catecholamine by the spleen and/or the liver partially counteracts this condition, it is necessary to answer three questions. (1) Does noradrenalin reproduce the effects of liver and spleen on the isolated heart? Does it raise cardiac efficiency by lowering myocardial oxygen consumption without raising cardiac work? (2) Are the catecholamines of the spontaneously failing heart or the perfusion fluid of these hearts depleted? (3) Does the addition of liver and spleen restore the concentration of noradrenalin in the heart or the perfusion fluid? It is known that the infusion of relatively large amounts of catecholamines diminishes the efficiency of the isolated heart; when catecholamines are infused at any fixed cardiac output, cardiac oxygen consumption rises in association with increases in blood pressure and heart rate, while the external mechanical efficiency of the heart declines. The fall in the percentage of oxygen extracted by the heart and the ratio of cardiac oxygen consumption to oxygen availability and the rise in coronary venous oxygen are all attributable to the direct action of the catecholamines on the coronary vessels.

However, the situation is quite different when very small amounts of noradrenalin or dopamine are used in these preparations. This results in an increase in the myocardial efficiency, because the oxygen consumption of the heart diminishes while cardiac work is not altered. This confirms previous studies of Krayer.

Is the heart muscle or the perfusion fluid in the heart-lung preparation depleted of noradrenalin? It has been mentioned previously that the heart contains appreciable quantities of noradrenalin. Experiments were performed in which the noradrenalin content of hearts rapidly removed from the animal was compared to that of the heart maintained in the heart-lung preparation for at least 1 hour. There is no appreciable difference between the two preparations. This finding illustrates that the presence of noradrenalin in the isolated heart does not prevent the development of spontaneous failure. This becomes particularly clear when the concentration of noradrenalin in heart muscle is increased by the addition of dopa to the perfusion fluid. It already has been shown by Euler that infusion of dopa into animals leads to considerable increase in the concentration of noradrenalin of the heart as well as that of other organs. Even after the positive inotropic effect of the conversion products of dopa (dopamine, noradrenalin, and adrenalin) has disappeared and the performance curve of the heart again shows the presence of failure, the concentration of noradrenalin in heart muscle remains elevated. Apparently "stored noradrenalin" does not affect myocardial contractility; similar to acetylcholine, it may be inactivated by special binding to proteins and only the nerve impulse can establish the link between the amine and the effector organ. Recent information indicates that the catecholamine content in the perfusion fluid of a heart-lung preparation is diminished. One may conclude therefore that the spontaneous failure of the isolated heart results from deficiencies of catecholamines in the perfusion fluid and that the amine content of the denervated heart is ineffective in preventing the development of failure.

Acute myocardial failure also can be observed in vivo, for example, in myocardial infarction and hemorrhagic shock. In the latter condition, observations on the effective atrial pressure, ventricular volume changes, and intraventricular pressures have demonstrated that the deterioration of myocardial expulsive power contributes to progressive circulatory failure, and that myocardial depression brings about the development of circulatory failure when transfusions are given after the development of an irreversible state (the normovolemic phase). In addition, the coronary flow diminishes during both the oligemic and normovolemic phase of hemorrhagic shock. These dynamic alterations result in definite disturbances in general metabolism, in which the heart is also involved. There is evidence of generalized systemic glycolysis, but the myocardial extraction of lactate is increased, indicating that the enzymatic pathways through which lactate is channeled are not interfered with by the myocardial ischemia. The concentrations of pyruvate in coronary vein blood are increased above those of arterial blood (negative myocardial pyruvate balance), and the myocardial extraction and usage of glucose are diminished.

Myocardial infarction also leads to acute myocardial failure if the uninvolved portion of the myocardium fails to compensate for the loss of contractile power of the ischemic muscle. Under these circumstances, there is a decrease in stroke volume and a compensatory increase in peripheral resistance. In experimental myocardial infarction the coronary flow and the myocardial oxygen usage are also diminished. Metabolic changes suggest that these dynamic alterations are accompanied by partial glycolysis in heart muscle. Pyruvate and lactate concentrations in coronary vein blood frequently exceed those in arterial blood. Myocardial glycolysis is also present in the arrested and fibrillating perfused heart. There is some evidence, therefore, that acute myocardial failure, whatever its origin, is accompanied by disturbances in the metabolism of the heart muscle. This disturbance in energy production conceivably may lead to diminished expulsive power of the heart and to progressive circulatory failure.

CHRONIC MYOCARDIAL FAILURE

Chronic myocardial failure is difficult to reproduce in the experimental animal, and results obtained in dogs with "chronic failure" may not be entirely applicable to man. It is now possible to study the extraction of substrates by the human heart with the help of coronary sinus catheterization. Using this technique, it can be demonstrated that the myocardial usage of oxygen, glucose, pyruvate, lactate, fatty acids, amino acids, and ketones is not different in patients with congestive heart failure, in individuals with compensated heart disease, and in those without evidence of heart disease. Values for the respiratory quotient are also identical in these groups. Since the mechanical work performed by the heart is usually decreased (except in high output failure), the failing heart appears to be deficient in its ability to utilize energy for effective muscular contraction. Further support for this conclusion has come from studies on the contractility of actomyosin prepared from normal and failing human heart muscle. The study of contractile proteins prepared from human hearts was made possible by the finding that the time interval (2 to 6 hours) between the death of the patient and the preparation of actomyosin does not affect the shortening of the actomyosin bands. It is found that the contractility of actomyosin bands prepared from failing human hearts is considerably less than that of patients with no clinical evidence of congestive failure. This furnishes additional evidence that in chronic clinical heart failure, the diminution in cardiac reserve results from disturbances in the contractile elements of the myocardium.

The exact nature of this disturbance is as yet uncertain. The pathologist is unable to find specific changes in heart muscle of patients who died in congestive failure. In dogs with chronic heart failure some differences in the protein composition in heart muscle have been found (Benson). Among these differences was a decrease in concentration of actomyosin, diminished viscosity per unit of actomyosin, and decreased viscosity response to the addition of adenosine triphosphate. These changes can be ascribed to alterations in the organization of actomyosin, more specifically, to the presence of myosin uncombined with actin. It has been observed also that heart failure in dogs leads to marked changes in the physical-chemical properties of myosin consistent with a sizable increase in molecular weight (Olson). The mechanical factors leading to diminished contractility of actomyosin prepared from failing human hearts are also obscure. Heart failure, whether acute or chronic, is accompanied by an increase in intraventricular initial tension and initial length. These in turn result from deficient emptying of the ventricle during systole and the consequent increase in the volume of residual blood retained. It seems possible, therefore, that a gradual increase in stretch of the myocardial fibers may be responsible for the alterations in contractile proteins which lead to diminished contractility. All efforts, however, to diminish the contractility of actomyosin bands by distention of the ventricle of dogs' hearts with balloons to pressures exceeding 180 mm. of mercury for 4 hours have been unsuccessful. It is possible that the changes in actomyosin can be produced only when the "stretch" persists over a period of months or years.

VOLUME RECEPTORS

The discussion has dealt with a multiplicity of factors which can lead to myocardial failure. It remains to be seen how this disturbance in the heart muscle can manifest itself in the general signs of heart failure, of which edema accompanied by sodium retention is the most important. One therefore must search for a connection relating the disturbances in the heart muscle with both the posterior pituitary and the renal tubules. Within recent years, the work of Gauer and his co-workers has furnished important clues as to these relationships.

It has been known for a long time that changes in blood volume can be accompanied by changes in urine flow. Small diminutions in plasma volume not sufficient to cause a detectable rise in blood pressure can lead to oliguria. On the other hand, small transfusions of plasma or whole blood lead to diuresis. These effects suggest a reflex arch, with a receptor organ, and an afferent and efferent reflex arch. Where are the receptors located? According to Aviado and Whitteridge and others, the thoracic vessels are amply supplied with receptors. If they play any role in perceiving changes in volume and transmitting them to the central nervous system, then changes in "central" blood volume should lead to alterations in urine flow. Working first on dogs, Gauer and his co-workers produced negative and positive pressure breathing and studied the effect on urine flow. They found that after a control period of constant urine flow, application of negative pressure breathing produced an increase in urine excretion of between 100 and 200 per cent. After cessation of the negative pressure, the urine flow returned gradually to control levels. In contrast, positive pressure breathing diminished urine flow. The diuresis produced by negative pressure breathing is delayed; while central venous pressure heart rate and respiration changed immediately with the onset and usually stayed constant for the period of negative pressure breathing, urine excretions increased only a little in the first 10 minutes, then rose faster and finally leveled off to a maximum after 30 to 50 minutes.

Human subjects, like anesthetized animals, also show an increased urine flow in response to continued negative pressure breathing. Sieker studied the renal excretion of water, sodium, and potassium, urinary pH, and the endogenous creatine clearances during negative pressure breathing. Continuous negative pressure breathing was associated in man with a water diuresis. Neither urine pH nor sodium and potassium excretion changed. The same mechanism postulated in the animal experiments (distention of the vascular regions in the thorax, which possess stretch receptors) was assumed to be operating in man. In addition, the role of the antidiuretic hormone was strongly suggested from these studies because the electrolyte excretion remained constant and the onset and cessation of the diuresis were gradual.

The question of the exact location of these receptors remained to be answered. It appeared likely that they are located in the thorax. Thus, they may be present in the right heart, the pulmonary artery, the pulmonary veins, and the left atrium or left ventricle. Experiments were performed by Gauer and co-workers in which stepwise engorgement of the intrathoracic vascular bed was produced. The pulmonary arterioles were obstructed by injection of plastic spheres into the pulmonary artery. This procedure, although leading to an increase in pulmonary artery pressure, was without effect on the urine flow. Obstruction of the pulmonary veins by snares placed around the pulmonary veins close to their entrance into the left atrium was equally without effect. In contrast, obstructive distention of the left atrium by a balloon led to a delayed increase in urine flow. Apparently, stimulation of the receptor situated in the left atrial wall led to afferent impulses in the vagus nerve. It was therefore suggested by Gauer and his co-workers that the left atrial receptor network plays an important part in the volume sensitive mechanism postulated.

Why is water retention present in congestive heart failure when, under these conditions, the left atrium is distended? One may assume with McLean that edema is a problem in physiological regulation and represents a perversion of the normal regulatory mechanism of volume. The assumption that a circulatory reflex mediated through stretch receptors may change its sensitivity and eventually result in a perversion of its normal function has been proved for other receptors such as the carotid sinus reflex. Apparently the state of contraction or the sympathetic tone of the vascular walls which carry vasosensitive elements determines their mode of action. Since it is generally believed that vascular tone is increased in congestive failure, one may consider that the sensitivity of the volume regulatory mechanism is decreased leading to fluid retention in spite of congestion.

What are the causes and mechanism of sodium retention in congestive heart failure? It should be mentioned that there are many causes involved in causing the kidney to retain sodium. There is the possibility of diminished glomerular filtration rate, the more likely possibility of increased tubular reabsorption of sodium, and increased secretion of adrenal steroids. Cuffing of the extremities, tilting of the head up position, and minor degrees of hypotension have a similar effect, whereas increases in blood volume and extracellular fluid produced in the recumbent position increase excretion of sodium by the kidney.

What are the mechanisms by which these responses are mediated? In this connection, aldosterone has received widespread interest. It has been known that in many clinical syndromes manifested by sodium retention and edema, the urinary excretion of aldosterone is markedly elevated. This is the case in congestive heart failure, cirrhosis, and nephrosis. Merrill has pointed out that the action of aldosterone, like that of other adrenal steroids, depends upon the physiologic situation in which it acts. Thus, aldosterone administered to a patient with adrenal insufficiency causes marked sodium retention and excretion of potassium. However, in the individual with normal adrenals, potassium loss may be marked but there is little sodium retention. In many instances, there is lack of correlation between the urinary excretion of aldosterone and sodium excretion. For example, in congestive heart failure, the administration of adrenal steroids may cause sodium diuresis which could not be correlated with the corresponding decrease in excretion of aldosterone (Merrill).

Definitive knowledge therefore is quite scanty concerning the direct stimulus to sodium retention. Assuming that nature does everything in the most direct way, one may assume that the main factor which governs sodium excretion is the volume of body fluids. According to Merrill, current evidence suggests that this is indeed the mechanism which controls aldosterone secretion by the adrenal cortex. The changes appear to be independent of the serum sodium concentration as evidenced by the fact that aldosterone excretion falls when in a salt depleted subject body fluids are expanded without addition of sodium. In the human, increased caval pressure produced by a balloon in the cava or by abdominal compression has been shown to result in increased sodium retention although aldosterone secretion was not measured. Whether this is mediated by renal nerves is as yet not clear. From similar experiments performed on the dog, the conclusion has been reached that aldosterone excretion and sodium retention may be a function of the volume of body

fluids acting through changes in venous pressure and venous tone. Congestive heart failure is accompanied by an increase in these parameters. Whether this is the only stimulus influencing aldosterone excretion and sodium retention remains to be seen.

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♦ Dr. Bing, Department of Medicine, Wayne State University School of Medicine, Detroit.

Women Weigh Less Now; Men Tend to Be Heavier

Women weigh distinctly less than a generation ago, while men tend to be heavier, according to a study published by the Society of Actuaries entitled, "1959 Build and Blood Pressure Study."

The study, said to be the largest statistical investigation undertaken in the health field, will change the weight tables now in general use, which were based on an actuarial study of 30 years ago. According to the society's findings, the weights of women in their twenties average at least 5 pounds less than three or four decades ago. Men weigh about 3 pounds heavier.

Variations in mortality and morbidity according to build were studied in nearly 5,000,000 persons covering 20 years' experience. Marked underweight is much less serious now than formerly, but excess mortality associated with overweight remains high. Men with weights 20 pounds above average incur a penalty of about 10 per cent higher mortality, while weights 50 pounds above average are associated with an excess mortality of up to 50 or 75 per cent. Women are able to stand added weight better than men. In both sexes the lowest mortality at ages over 30 is found among those 15 to 20 pounds below average weight. Main causes of death among overweights showed marked increased mortality first in diabetes and certain digestive diseases as weight increased. With further additions to weight, death rates from heart disease rose sharply.

The actuarial study also showed increased blood pressure to be a danger signal.

Atherosclerosis

Some Present Day Concepts and Some Attempts at Control Of Hypercholesterolemia

GEORGE R. HERRMANN, M.D.

Galveston, Texas

CORONARY atherosclerosis is the grim reaper whose scythe hangs as the sword of Damocles by a hair over our heads. It is the silent headsman who waits year out, year in, as the fates spin; Clotho draws life's threads, for Lachesis to twist and Atropos to sever. It is the captain of the men of death, the swift executioner of the great and the small, the cynical cavalier of deeds well done, glories won or to be won, the fury Tisiphone of the prematurely vulnerable and sinful, but *not* the inevitable Nemesis of naturally aging man.

I have used the characters of Greek and Roman mythology to emphasize how much is in the hands of the gods, the fates, and the furies. Heredity plays a significant role in our destiny, and chronic, emotional, or tension states are probably additive. The foibles of man are now thought to contribute so much that the coronary catastrophe no longer can be ascribed to the overextending of a man's laudable virtuous acts and must be attributed to his indiscretions.

"Atherosclerosis is near to the heart of every man and eventually every woman too," and along with hyperpiesia is the great challenge of modern medicine. Atherosclerosis has been the subject of a tremendous amount of research, and a mass of literature of experimental and clinical data, much of which is contradictory, has been accumulated. Most of the problems have not yet been solved. It now seems to be high time to take stock to determine what has been established, in what directions we are justified in proceeding with some hope of success, and what we may accomplish.

There is at the present time no specific blood chemical or lipid tolerance test for the early detection of atherosclerosis. We must rely upon some diagnostic combination such as (1) a bad family history for arterial disease, (2) a dietary history of indiscretions, (3) visible changes in the lumens of the

From the Cardiovascular Research Laboratory of the University of Texas Medical Branch. Supported in part by grants-in-aid from Ciba, Inc., Sandoz, Inc., Wyeth, Inc., U. S. Vitamin Corp., and the H. H. Weinert Fund.

retinal arteries, and (4) elevated total blood lipid, cholesterol, phospholipids, and beta lipoproteins. On the basis of the presence of all of these, we may justly infer that atherosclerosis probably has begun and that the major arteries have been or in time will be involved at buffeted areas such as bifurcations in the coronaries or cerebral arteries.

Within the past few years, statistical scientists, therapeutic nihilists, have blasted some of our most cherished clinical hopes, and we may no longer assuage our patients who have had an attack of coronary thrombosis that they are victims of overambition, overconscientiousness, overwork, long hours, chronic tension states, worry, and shock. We must now reproach our atherosclerotic patients for a poor choice of their ancestors and for overindulgence in rich foods, tobacco, leisure, and physical laziness—in other words, gluttony and indolence. It is no longer considered good medication to prescribe brandy, and all coronary vasodilators are declared to be of doubtful value and all drugs are useless except for the psychotherapy value. The nihilists insist that when the diagnosis can be made, it is already too late for the dietary restrictions of fat, as it is for the choice of our ancestors. In this state of confusion, we must walk backward into the future, review the history of the subject, and retrace the halting steps of the progress of our knowledge of atherosclerosis.

HISTORICAL

We have learned that atherosclerosis was present in ancient peoples, and unquestionable evidence of the disease has been demonstrated in the Egyptian mummies of the earliest dynasties. Atherosclerosis apparently was considered as an inevitable part of the aging process, and little attention was paid to it until the nineteenth century, when the pathologist Rokitansky[21] reported his concept that atheromatous plaques were the result of the laying down upon the intima of substances from the blood. Virchow[23] differed sharply with this idea and described two types of lipid disturbances as fatty degeneration, which he considered a cellular metabolic disorder, and fatty infiltration, which he attributed to a disturbance in the transport of the lipids. Triglyceride globules in the cells were considered evidence of metabolic disturbances while degenerating phagocytes and depositions of lipids in the interstitial tissues indicated abnormal transport. Anitschkow[3] produced atheromatous-like lesions in rabbits by cholesterol feeding. Much chemical study of atheromatous lesions was carried out in the early part of the twentieth century by experimental pathologists.

Leary[16, 17] renewed interest in cholesterosis by demonstrating histiocytes laden with lipids and cholesterol crystals passing through the intima possibly attracted by chemotaxis. In the last decade and a half, atherosclerosis has rapidly assumed an important place in modern experimental and clinical investigation. Yamagiwa and Adachi[25] found a natural atherosclerosis in chickens. Fox[6] noted the natural atherosclerosis in birds. Domestic animals, like rabbits, were found susceptible[9] to the production of lesions by cholesterol feeding similar to but not exactly the same as human atheromatous plaques. Steiner[22] was successful in producing atheromatosis in dogs with fat feedings only after the thyroid had been depressed greatly with thiouracil. Rinehart[20] produced atheromatosis in pyridoxine deficient monkeys by the feeding of cholesterol and a high fat diet. It was not until very recently, 1955, that Hartroft and Thomas[8] succeeded in producing atheromatosis that resulted in myocardial infarction in rats that had been fed thiouracil along with excessive amounts of butter, bacon, and cholesterol. Werthessen[24] demonstrated lipid metabolism in the calf's aorta and found that the aorta of the baboon, like that of man, does not synthesize lipids, as do the aortas of all animals below the primates.

Dr. George R. Herrmann, director of the Cardiovascular Research Laboratory at the University of Texas Medical Branch, presented this address at the First Medical Congress of the University of Puebla, Mexico, on July 15, 1958, and at the Texas Heart Association in San Antonio on April 18, 1959.

Although the pathogenesis of atherosclerosis has not been established, data on the blood lipid levels of more than 500 patients suggest that decholesterolizing procedures are worth while. Restriction of animal, dairy, and hydrogenated fats and substitution of poly unsaturated fatty acids is practical. Niacin in massive doses, phenyl ethyl acetoamide, and diethanolamine also show promise.

FACTORS IN ATHEROGENESIS

Probable contributory factors in atherosclerosis also have been established by extensive clinical studies and in clinical and hormonal investigations. Inherited endocrine metabolism may play an important role. It seems that some families have a vascular protoplasm abnormality or enzyme systems in the arterial walls that have an avidity for or an abnormal ability to produce abnormal lipids locally in the subintima. There occur familial tendencies to general lipid metabolism disorders through abnormal hormonal effects from the pituitary, thyroid, pancreas, or ovaries resulting in hyperlipemia or hypercholes-

terolemia.[12] Cholesterol, which is insoluble, and beta lipoproteins, which are only slightly more soluble, are usually increased. The more soluble alpha lipoproteins may be decreased. The less soluble large chylomicrons, beta lipoprotein molecules, and those of the higher flotation rates Sf 70-100 are considered to be atherogenic.

HISTOPATHOGENESIS

Lipid laden endotheliocytes, histiocytes, or phagocytes may be increased and may penetrate the intima and break down in the subintimal tissues.[4, 13] The fibroblastic elements in the arterial wall of some patients may have, according to some recent experiments, unusual avidity for saturated fats. Thrombophilia may give rise to intimal plaques.

The permeability of the intima may well be an important factor, since permeability is increased by anoxia incident to vasa vasoral mural ischemia. Chemotaxis may play a role. The augmented fluctuating blood pressure or turbulence of hypertension may mechanically implement the penetration of the intima in the affected areas by serum albumin lipids, triglycerides, chylomicrons, and histiocytes laden with cholesterol. Local lipids may result from the breakdown of thrombi or of the red cells under the intima, depositing insoluble cholesterol in situ, which the enzyme and transport system, through the mural lymphatic mechanism, seemingly cannot remove. The accumulation of these results in the formation of the nidus of the atheromatous plaque. This histogenesis of the subintimal atheromatous plaque by the infiltration of lipids at the point of increased permeability from turbulence seems logical, but is probably an oversimplification.

In the very earliest lesions, the lipids are in the same ratio that they are in the serum plasma; but the most soluble ones seem to be metabolized locally or transported and the highly insoluble cholesterol persists and increases in relative amount, resulting in the slow growth of the plaque by small increments. At first, it seems as though nature has produced a cushion of the turbulent blood flow against the buffeting. There is, however, in these same areas, evidence of some cellular infiltration, local cell degeneration, and production of mucoproteins and acid polysaccharides; later, necrobiosis, collagen deterioration, and proliferation of fibroblasts; and still later, calcium deposition.

Intramural hemorrhage may result in a rapid increase in the size of the plaque, and this may cause sudden occlusion of the lumen of the artery. The bulging plaque may split the intima; then the roughened area may gather fibrin and produce a local thrombus, or the extrusion of pultaceous grumous material and thromboplastic substances from the plaque may result in local intravital clotting and thrombotic occlusion. A high content of plasma lipids seems to cause some sludging of the blood, which increases the tendency to thrombosis and inhibition of the fibrinolysins.

CLINICAL INVESTIGATIVE APPROACH

The natural history of atherosclerosis must be documented. In this the practitioner may contribute a great deal of valuable information. A physician established in a community that is more or less stable is in a position to learn much about this disease. Unfortunately many communities in this country have a somewhat floating population. We must hope for more stabilization of our people in the future in smaller self sufficient towns. We may have had to depend too much upon practitioners in other countries who follow their patients and their families from the cradle to the grave. There are, however, certain well organized long term atherosclerotic studies in the United States such as the Framingham study and the Armed Forces records, especially the observations of personnel in the Air Force Medical Corps over the years, which will yield valuable information as time goes on. Industry, business, and insurance company data, as well as community reports, may be helpful in accumulating information as to how much emotional stresses or occupational strains or chronic tension states contribute to coronary artery disease. Studies of the incidence of atherosclerosis in isolated groups such as those living under stress as contrasted to those who are serene, tranquil, imperturbable, and composed, or those living a sedentary life as compared with those who are very active in athletics or taking regular exercises are important. In order to get more satisfactory information, it seems that we should include repeated total blood cholesterol determinations as a part of the study of every patient over the age of 30 years.

In those in whom a hypercholesterolemia has been established, we should observe the effect on the patient and on his blood lipid levels of (1) no restrictions and no therapy, (2) decreased ingestion of animal fats, (3) phytosterol blocking the absorption of fats, (4) estrogenic conversion, (5) increasing the oxidation by nicotinic acid or vitamin B_2, vitamin A, pyridoxine, or vitamin B_6, and/or (6) substitution of the unsaturated fatty acid, and (7) attempting to inhibit the synthesis of endogenous cholesterol in the liver. We should note whether these patients with therapeutically lowered cholesterol levels have fewer symptoms and signs or less

evidence of atheromatous disease than do the controls.

DECHOLESTEROLIZATION

Decholesterolizing procedures in man have been questioned as to validity and as to value when accomplished. It has been pointed out that there is no justification as yet for a mass population change in the American diet or way of living in order to lower the high blood cholesterol levels. In spite of many studies, there is no absolute proof that the lowering of the blood cholesterol will have any salutary effect in atheromatosis in man. There is no reliable evidence in man that there has resulted prevention of increase in size of atheromatous plaques or rupture of atheromatous plaques that previously had formed. However, most patients get symptomatic relief on dietary fat restriction, and anginal attacks are ameliorated.

Diet.—Vital statistics and insurance company data have given evidence of increased prevalence of degenerative heart and artery disease in the overweight or in the obese patient. It is therefore considered justifiable to prescribe the reduction of excessive body weight by a low fat and low calory diet and the maintenance of the ideal weight by increased exercise of walking ½ mile three times a day. The caloric value of the diet may be lowered by reducing the fat content to 25 to 30 per cent of the total calories. Furthermore, substitution of unsaturated fatty acids for two-thirds of the low (25 to 30 per cent) fat calories of a 1,500 to 2,000 total calory diet is in order certainly in patients who have an established or extreme hypercholesterolemia.[14] A positive family history of coronary or cerebral arterial disease with or without some hypertension is reason enough alone for restricting the fats of animal and dairy origin in the diet. The substitution of vegetable oils, as corn oil or soya oil made up chiefly of the essential poly unsaturated fatty acids for at least 20 per cent of the restricted fat calories (30 per cent of the total calories) is considered good and rewarding practice.

Drugs.—In addition to the reduction of the exogenous intake of animal fats in the diet, the use of the phytosteroids such as Cytellin to block the absorption from the intestinal canal of the exogenous and also the reabsorption of the endogenous cholesterol that is present in the bile has reduced blood lipid levels slightly. The increased oxidation of lipids with massive doses of nicotinic acid if tolerated seems to be a practical therapeutic method, using the slowly released niacin preparation to prevent side effects.

It has been demonstrated that when the exogenous intake of fats and the plasma lipids are decreased, the endogenous synthesis may be increased. Therefore one may attempt depression of the endogenous synthesis by phenyl ethyl acetoamide or alpha phenyl butyramide or diethanolamine. There may be accomplished a decrease of the total, but particularly the beta lipoprotein fractions by the use of natural estrogens such as Estinyl or Premarin and synthetic chlorotrianisine such as MER 13 and 29. It would seem desirable to reduce the high ratio of beta to alpha lipoproteins. This result is not of established value. The side effects, gynecomastia and impotence, which are not acceptable to many men, may be minimized by low dosage and by the use of synthetic nonfeminizing sex hormones.

TEXAS STUDIES

My early studies were of the blood cholesterol and blood lipid levels in health and in various diseases. I have been so impressed that I have had blood lipid studies done routinely on every private patient entrusted to me during the last several years. This report is on the data from these patients. My first report[10, 11] was based on observations made for the most part on charity ward and clinic patients. Similar data have been supplied from many clinics throughout the world. Evidence seems to be sufficient to justify the contention that elevated blood cholesterol, hyperlipemia, and high beta lipoproteins play a prominent role in atheromatosis. Animal experiments that I have carried out, as many others have, seem to substantiate this opinion. The data to be reported herewith seem to be in agreement.

High blood lipid levels have been shown to be susceptible to various therapeutic procedures, and an attack on this aspect of the problem seems to be our most rational approach. However, I have never felt that the elevated cholesterol, lipids, and fats constitute the only problem, nor that the pathological processes would be entirely removed by returning the lipids to normal levels. All the possible contributing factors of atheromatosis must be considered and investigated, and if any are present, treatment should be directed toward them.

However, the disturbed fat metabolism has seemed to me to be a prominent significant factor and the most rational, most responsive, and most easily measurable by clinical means. I have undertaken such studies and have advocated the sharp restriction of the intake of animal fats and dairy fats. The reduction of the total caloric intake, of body weight, and of the blood cholesterol levels has yielded salutary effects, possibly psychotherapeutic, in that there has resulted in most patients a feeling of well being. Most of my patients follow the diet in principle; to some, of course, a prescribed diet is primarily a

conversation piece. The patient must be strong willed, almost a fanatic, dedicated unswervingly to observe the extremely sharp restrictions, year in and year out. In such some harm may result from imbalances or inadequacies especially if supplemental vitamin A intake is neglected, and an undesirable nutritional disorder may be added. The great question is whether or not atheromatosis in general is amenable to the lowering of blood cholesterol. Most of the patients referred to me in the last few years had been placed on restriction of their dietary fat intake, but in most of them hypercholesterolemia persisted.

SUMMARIZED DATA OF PRESENT STUDY

These data were obtained from slightly more than 500 private patients referred by their physicians for study because of cardiovascular complaints. Many had been observing some restriction of the animal and dairy fats in their diet. The blood lipid fractions, total cholesterol, organic phosphorus, phospholipids, and the alpha and beta lipoproteins have been determined. In this series (fig. 1) there were 106 patients, 72 males (averaging 43 years) and 34 females (averaging 45 years), who presented no clinical evidence of heart disease and served as controls, along with 14 patients, 8 males (26 years) and 6 females (35 years), with congenital heart disease and 19 patients, 11 males (32 years) and 8 females (30 years), with rheumatic heart disease, practically all of whom were in the preatheromatous age groups. The patients with rheumatic heart disease had somewhat elevated blood lipid levels as did also 47 hypertensives, 28 males (51 years) and 19 females (49 years), who had shown no signs of heart disease or even suggestive evidence of aortitis. The 20 oldsters, 16 males (66 years) and 4 females (65 years), who showed clinical evidence of cerebral arterial disease primarily, had only moderately elevated blood total cholesterol and phospholipid levels and high beta lipoprotein levels.

In a group of 74 patients with signs of aortitis, 45 males (average 57 years) and 29 females (59 years), without or with hypertension, abnormally high mean values for cholesterol, phospholipids, and

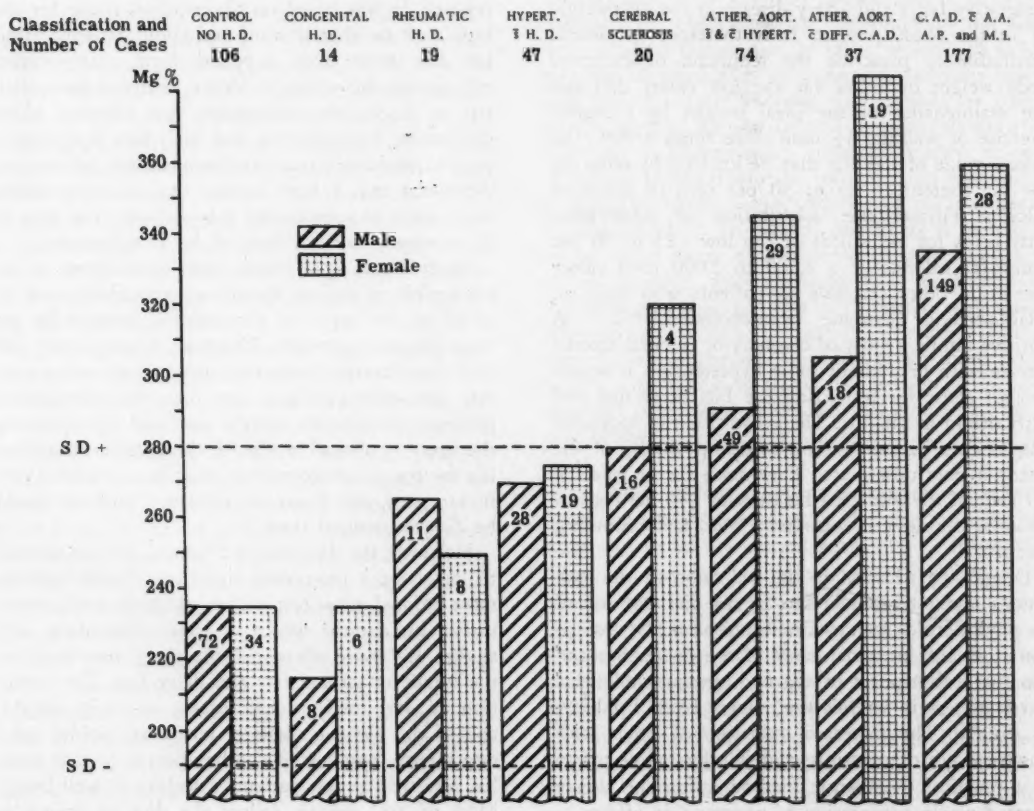

Fig. 1. Mean total cholesterol values in various conditions in male and female patients.

beta lipoproteins were recorded. A group of 37 more who presented signs of aortitis and additional electrocardiographic evidence of diffuse coronary artery disease, of whom there were 18 males (59 years) and 19 females (53 years), showed still higher blood lipid levels.

The 177 patients, 149 males averaging 54 years and 28 females averaging 59 years, who presented clinical evidence of coronary artery disease with angina pectoris and/or myocardial infarction showed the very highest levels of total cholesterol and beta lipoproteins. The 5 to 1 ratio of men to women is rather greater than usual, probably due to the fact that the men as responsible heads of families seek relief and advice more often than do women. All of these data are set down in table 1.

DISCUSSION

The total cholesterol esters, organic phosphorus, phospholipid fractions, and alpha and beta lipoproteins were determined. In this series of 500 patients, personally followed, there seems to be correlation between the presence of evidence of atheromatous disease of various grades and the levels of the blood lipids. Rheumatic heart disease patients and hypertensives with no signs of heart disease had rather high levels of cholesterol and phospholipids. Those with cerebral sclerosis primarily showed less high levels than those with atheromatous disease of other arteries. Practically all of my patients who presented signs of coronary artery or ischemic heart disease had very high blood cholesterol levels. The few exceptions with normal or only slightly elevated cholesterol levels had high (76 per cent plus) beta lipoproteins and less than 24 per cent alpha lipoproteins.

In spite of the total absence of any proof that lowering of levels of blood cholesterol, phospholipids, and beta lipoproteins has any definite beneficial effect on atheromatous lesions, nevertheless, steps to this end, I believe, are for the time being amply justified. Therapeutic efforts have been directed toward reducing the hypercholesterolemia.

THERAPEUTIC UNDERTAKINGS

The blood lipid pattern changes have been determined in about 50 long term (1 to 3 month) studies of patients on low animal and dairy fat diets. They range from conspicuous lowering in only a few patients who were fanatical dieters to no changes in many of the patients. A tabulation of the data recorded is presented in table 2 and will be discussed.

The first approach was naturally a sharp reduction in the patient's dietary intake of animal fats. The effects of low animal and low dairy fat diets on patients were noted. A decrease in the total blood cholesterol and fractions was found in a large percentage of the very cooperative patients who had carried out the restrictions religiously, especially in those who had lost weight. However, few patients persistently adhered closely to the 30 per cent fat calories diet. There were some patients in whom the low fat diet alone had produced little or no lowering of total plasma lipids nor of the more atherogenic fraction. Some considered the diet prescription a sheet to talk about, giving it lip service only. It was evident in several patients that the total serum lipids and fractions could be reduced by a very sharp restriction in the intake of animal fats and avoidance of dairy fats and replacement of two-thirds of the allotted 30 per cent fat calories with unsaturated fatty acids, but the restrictions were distasteful to some, difficult to carry out, and occasionally apparently not rewarding.[10, 11]

The second attack, it was thought, might well be directed toward improving the liver metabolism of fats. In these patients, I prescribed along with the dietary restriction, the addition of choline, methionine, inositol, vitamin A, vitamin E, vitamin B_6 or pyridoxine, and vitamin B_{12}. On this regimen, there usually were further slight reductions in the blood fat levels, but the changes were apparently not statistically significant. The patients felt better, especially those who had lost some weight. The improvement was probably for the most part a psychotherapeutic effect.

Phytosterols were suggested for reduction of the blood lipids by prevention of the absorption of cholesterol. Phytosterols which are less metabolizable

TABLE 1.—*Blood Lipid Levels in Persons with No Heart Disease, with Heart Disease, and with Atheromatosis.*

Diagnosis	No. Patients: Total	No. Patients: Male/Female	Av. Age (Yr.)	Cholesterol (mg./100 cc.)	Phospholipids (mg./100 cc.)	Beta Lipoproteins (%)
No heart disease	106	72/34	46	236	283	85
Congenital heart disease	14	8/6	26	223	215	64
Rheumatic heart disease	19	11/6	31	254	242	74
Hypertension without heart disease	47	28/19	51	271	246	83
Cerebral vascular disease	20	16/4	66	307	267	56
Atheromatous aortitis	74	49/29	58	311	274	82
Coronary artery disease, diffuse	37	18/20	56	339	293	87
Coronary artery disease, angina pectoris, and myocardial infarction	177	149/28	57	339	283	89

were found to compete with the animal sterols and block absorption. Sitosterol had to be given in double tablespoonful doses, ½ to 1 hour before each meal. Sitosterols were introduced under the trade name of Cytellin, and this product was administered to 7 of my patients. They took the preparation in full ounce doses 1 hour before meals for an average of 84 days. In these patients, Cytellin was found to reduce the total lipid levels 10 to 20 per cent, but the average reduction was 13 per cent (table 2). Other drugs that change the intestinal conditions or flora such as neomycin have been found to be more effective.

Estrogens have been found to reduce the most atherogenic fractions of lipids. It has been noted repeatedly that up to the age of 50 years, men have higher levels of serum lipids than do women of the same age, but as women approach and pass the menopause, they show steady increase in the serum lipid levels and reach or supersede those of men after the age of 50. It also has been noted that men up to the age of 50 have higher levels of beta lipoproteins making up more than 75 per cent of the total with alpha lipoproteins less than 25 per cent. In some atheromatous coronary occlusion cases the beta lipoprotein level has amounted to 80 to 90 per cent or more of the total. Estrogenic substances, especially estradiol, Estinyl, and Premarin, have been found to lower the beta lipoprotein percentages to normal in animals, and somewhat similar results have been observed in some men. The amount of estrogenic hormone necessary, however, was such that some side effects as feminization, especially gynecomastia and loss of libido and potentia, developed in men. The breast lesions have been reported to progress to malignant tumor formation.

Biochemists have spent much time and energy in the attempt to produce a nonfeminizing female sex hormone. I was supplied with a synthetic chlorotrianisine, MER 13 and 29, which I used in 9 studies, each, MER 13 for an average of 83 days and MER 29 for 35 days. There resulted after MER 13, in doses of 250 mg., an average reduction of 14 per cent in total cholesterol, 14 per cent in the phospholipids, and 3.5 per cent in the beta lipoproteins. These changes again were not significant enough to warrant a large scale production of this preparation for general use. However, MER 29 in doses of 250 mg. three times a day was used in 9 patients for 30 to 40 days and produced 15 to 40 per cent (average 25 per cent) reduction in total cholesterol but little change in phospholipids and 4 per cent reduction in beta lipoproteins.

Unsaturated and essential fatty acids as in corn oil were found to be much less atherogenic than the mixtures of solid saturated fats as lard, suet, and hydrogenated oils.[15] My miscrediting of the effects of corn oil to methionine, choline, and inositol in experimental hypercholesterolemia was realized when evidence was gradually accumulated that poly unsaturated fatty acids such as essential double bonded linoleic, linolenic, and arachnidonic acids of corn or fish oils have reduced serum cholesterol levels. There has been reported support for this concept by many investigators. In our studies at Galveston we had placed in our low fat diets, corn oil and soya oil from the beginning to supplant saturated hydrogenated solid animal, dairy, and vegetable fats whenever it was possible. In my experiences capsules of unsaturated fatty acids as mixed linoleic sunflower or safflower oil merely added as supplements to the dietary were inadequate and produced only slight depressions of cholesterol levels. It must be admitted that the dosage in these instances was rather small. The amount of unsaturated fatty acid probably must be about 50 Gm. per day or 20 per cent of the total calories or two-thirds of the fat calories when they are 30 per cent of the total.

In our studies 2 or 3 capsules three times a day of Lufa or Safferol, each one for an average of 98 days, showed only a 2 per cent lowering of the total cholesterol, a 3.5 per cent lowering of phospholipids, but 30 per cent change of the significant beta lipoprotein fractions. The U. S. Vitamin Corporation has been aware of this and for several years has been submitting various unsaturated fatty acids and mixtures to us for clinical trial including Lufa and Safferol. Other pharmaceutical houses hurriedly put on the market preparations of unsaturated fatty acids of the essential type to be taken along with the usual meals, and these were thus offered as supplements to the diets. Kinsell,[15] who first reported salutary effects of unsaturated fatty acids, pointed out, however, that it was frequently necessary completely to replace for a time all saturated fats in the diet by

TABLE 2.—*Effect of Various Agents on Blood Lipids.*

Agent (Trademarked Name)	No. Cases	No. Days Therapy	% Decrease After Therapy		
			Cholesterol	Phospholipid	Beta Lipoprotein
Phytosterol (Cytellin)	7	84	13	11	4
Nonfeminizing estrogen (MER 13)	9	83	14	14	4
Unsaturated fatty acid (Safferol and Lufa)	12	98	4	3.5	3
Niacin (Nicospan)	57	52	21	13	6
Phenyl ethyl acetoamide (Natol)	3	14	20	20	11
Diethanolamine (MER 29)	9	35	25	5	4

unsaturated fats and also to replace considerable portion of the concentrated carbohydrate with unsaturated fats in order to achieve lowering the blood lipids initially. Soya margarine (Mar Parv) and corn oil margarine (EmDee) have been offered as substitutes. Once the salutary effect had been produced, it was frequently possible to liberalize the diet gradually by including slowly increasing amounts of saturated fats. The program for each patient had to be individualized.

Nicotinic acid has been found to be a succe[illegible] method of reducing blood fat cholesterol levels by augmented oxidation with vitamin B and A. Altschul[1, 2] had observed that oxidation of cholesterol reduced its atherogenicity in experimental animals. Methods of oxygenation were found to decrease serum cholesterol in many patients. Altschul proceeded to try to enhance the oxidative processes in the human body by stimulating the action of the respiratory enzymes. Nicotinic acid or niacin was chosen because it increased the concentration of respiratory coenzymes I and II in the blood of humans, and its use in massive doses was encouraged by the psychiatrists' administration of huge doses of niacin without any toxic effects. Altschul prescribed very large doses of niacin, 1 Gm. or more for each 50 pounds of body weight, and noted a consistent lowering of blood cholesterol.

I have used a slowly released niacin, MRD 505, 506, 507, and 507A (Nicospan), in 0.5 to 1 Gm. doses four to eight times a day. I found niacin to be ineffective in total doses of less than 2.0 Gm. per day. It is noted in table 2 that in 57 studies, which averaged 52 days each, there was an average drop of 21 per cent in total cholesterol, 13 per cent drop in phospholipids, and 6 per cent drop in the beta lipoproteins percentage of the total lipoproteins. It seems to me that Nicospan, which is fairly well tolerated even in those who have reactions to 50 mg. of niacin, was most promising of the decholesterolizing agents and well worth continuing. The ultimate question has not yet been answered as to whether or not the lowering of serum cholesterol levels in any way influences favorably the course of atherosclerosis. However, the patients have shown no signs of hepatic toxicity and feel distinctly better and are often relieved of angina pectoris attacks, which again may be a psychotherapeutic effect.

PEAA or phenyl ethyl acetoamide, 400 mg. three times a day, for the partial suppression of exogenous cholesterol formation in the liver, by interference with transmethylation at the mavelonic acid stage, has been used under Sodi-Pallares in Mexico by Nava, Comesaña, and others[18] along with nicotinic acid, 100 mg. three times a day. Good decholesterolization and no toxic effects were noted in their series in dogs and humans. I have used this in only 3 patients who could not take niacin in massive doses and who seemed to be refractory. Within 14 days I noted depression of total cholesterol by 20 per cent, phospholipids by 20 per cent (occasionally much greater depression was noted), and beta lipoproteins by 11 per cent. This seems encouraging and warrants further careful study with observation as to liver function before and at 2 week intervals during treatment. MER 29, which contains diethanolamine as well as the synthetic estrogen chlorotrianisine, similarly may depress endogenous cholesterol production.[11a]

The problem seems to be much the same as that of the modern therapy of hypertension, the cause of which likewise is unknown and the exact mechanism of drug action for which has not been determined. Nevertheless, there are drugs which will reduce tension, and it seems best now with our knowledge of the natural course of the disease to reduce blood pressure and likewise hypercholesterolemia when present. Our therapeutic attempts should be directed against any and all possible contributory factors.

There is, of course, not yet justification for attempting to change the dietary of the whole North American population. However, members of families in which there has been a high incidence of premature aging or atheromatous coronary general or cerebral vascular disease at an early age and who show high blood lipid levels justifiably may be advised to submit to restrictions and treatment which promise to lower blood lipids.

Patients who have suffered from angina pectoris or cerebral episodes or intermittent claudication and who are thus prematurely aged and who also have high blood lipid fraction most certainly should be treated by measures to reduce hypercholesterolemia or the high levels of supposedly atherogenic lipid fractions in the blood serum.

SUMMARY

Some presently held concepts and theories of the causes of atherosclerosis have been reviewed briefly. Data on the blood lipid levels of slightly more than 500 private patients seen in consultation and personally examined seem to support the thesis that hyperlipemia is an important factor in atherosclerosis.

Some contributory factors such as heredity, mesomorphism, chemical enzymes, hormones, anatomy, circulatory turbulence pressure, intimal trauma or injury, permeability, penetration of serum, albumin and fibrinogen and thrombin serum lipids, hypercholesterolemia, histiocytes laden with insoluble cholesterol crystals and fat globules, and local degenerative intimal and subintimal factors have been dis-

cussed. Thrombophilia with intimal involvement may be primary.

It is admitted that the pathogenesis of atherosclerosis has not been established; yet the most probable hyperlipemia factors are considered significant enough to warrant attack by therapeutic decholesterolizing procedures, especially in patients with clinical evidence of coronary or cerebral artery atheromatosis as the cause for ischemia. There is as yet no proof in man that lowering blood lipids decreases atheromatosis; however, symptoms are relieved.

The results of therapeutic attempts have been moderate with (1) decreased animal fat intake and (2) the blocking absorption with phytosterol or Cytellin administration, (3) the changing of lipoprotein patterns by natural female sex hormones or synthetic chlorotriansine such as MER 13 or 29, and (4) decreasing of atherogenic lipid levels by augmented unsaturated fatty acid chemical lipid metabolism. (5) The cholesterol depressing effects of oxidation by administration of massive doses of slowly released niacin (Nicospan) in patients have been highly encouraging while (6) the suppression of endogenous liver cholesterol formation with phenyl ethyl acetoamide (Natol) or diethanolamine (MER 29) may prove exceedingly advantageous if these preparations are no more toxic than they appear to be at this time.

The restriction of the intake of animal, dairy, and hydrogenated fats and the substitution of poly unsaturated fatty acids for at least two-thirds of the 30 per cent of calories allowed to fats is practical and rational in patients or potential patients. The therapeutic problem is about the same as is that of essential hypertension; the cause and rate of progression of both are still obscure and the exact machanisms of certain drug actions are still undetermined.

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Dr. Herrmann, Cadiovascular Research Laboratory, University of Texas Medical Branch, Galveston.

Nurse Training Programs Approved

As a result of the examination held by the State Board of Vocational Nurse Examiners, October 31 in Austin, three new vocational nurse training programs were approved, bringing a total of 105 active programs in Texas.

The new programs were approved at the Terry County Hospital, Brownfield; Cogdell School of Vocational Nursing, Snyder; and the Hamilton County General Hospital, Hamilton.

At the statewide examination, 637 candidates passed and were issued vocational nurse licenses. There were 73 approved vocational nurse training programs represented in the October examination. There were 8 candidates who qualified through their 2 years' training in professional nurse programs rather than by a year's vocational nurse training. At this meeting, 17 licentiates from other states were granted reciprocity licenses.

During the year 1957-1958, Texas graduated 1,236 vocational nurses, according to a recent report from the National League for Nursing. This is the greatest number of practical nurses trained by any of the states, and is 10 per cent of the national total. Since the inception of the vocational nurse law in 1951, a total of 21,260 licenses have been issued.

The next state board examination will be held in two sections—March 25 and 26 in Austin. Deadline for submitting applications for this examination is midnight, February 23. Inquiries concerning applications may be addressed to the State of Texas Board of Vocational Nurse Examiners, 1008 State Office Building, Austin 1.

Abdominal Aortography

COLVIN H. AGNEW, M.D. and ROBERT N. COOLEY, M.D.

Galveston, Texas

DOS SANTOS and his associates[17] developed the technique of translumbar aortic puncture and were the first to perform abdominal aortography (1929). Aortic puncture was done using local anesthesia, but because of pain produced by the irritating contrast substance then available (sodium iodide and Abrodil), general anesthesia was induced during the injection. By 1931 more than 400 examinations had been performed, and dos Santos and his group[16] published a book describing their experience and showing a number of conditions, mainly urological, that were susceptible to diagnosis by this relatively innocuous procedure.

Despite this extensive pioneer work, lumbar aortography received little attention in this country until Doss and his associates of Fort Worth and Nelson[12] of Seattle made preliminary reports describing their personal experience. It is fitting to recall that Doss, Thomas, and Bond[5] presented their original paper before the annual meeting of the Texas Medical Association 17 years ago. Although both reports were enthusiastic concerning the possibilities of the procedure and both found it essentially safe, it still received little attention until about 1947, when Wagner and others[20] reported on a sizable series of examinations without mortality or significant morbidity. Since then, the increasing number of reports in the medical literature indicates its widespread use.

Castellanos and Pereiras[3] found in 1940 that the lower abdominal aorta could be visualized by injecting contrast substance retrograde through a cannula inserted into the femoral artery similar to the method they used in the thoracic aorta. A year later Fariñas[7] described a similar approach except that he inserted a ureteral catheter in a retrograde fashion through the cannula inserted into the femoral artery. The catheter could be threaded into the abdominal aorta, and injection could be made at any preselected level. Fariñas called his procedure "selective arteriography." Goodwin and others used a similar approach except that they exposed the femoral artery and used a somewhat larger Cournand intracardiac catheter. Others including Pearl and others (cited by Bierman and others) have approached the aorta from above using the carotid, brachial, or radial artery and have used catheters with a suitable fixed curve.

Peirce[14] punctured the femoral artery and inserted polyethylene tubing through the cannula in a retrograde direction into the abdominal or thoracic aorta. Sufficient quantities of contrast substance then could be injected through the tubing to produce a satisfactory aortogram. Hooks and others reported also on the use of this procedure. More recently Seldinger[18] and Ödman[13] have revived the use of this technique by developing larger more maneuverable radiopaque catheters and have been able in many instances to do true selective arteriography by catheterizing the major branches of the abdominal aorta.

Robb and Steinberg[15] in their classical paper on angiocardiography reported that they had deliberately used this procedure to visualize the renal arteries. Leigh and Rogers emphasized its usefulness, and Porporis and others have used radioactive iodine (I-131) in tracer amounts mixed with contrast substance to determine the optimum time for abdominal filming.

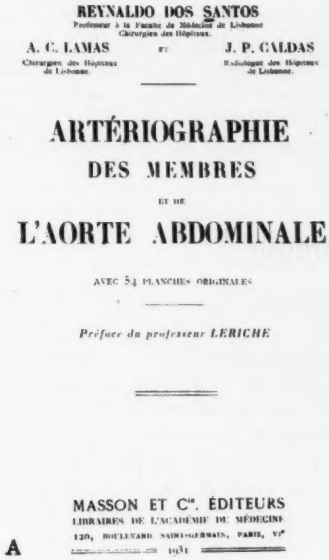
TECHNIQUE

Translumbar Aortography.—Local anesthesia can be used for translumbar aortography in most instances particularly if the confidence of the patient is obtained by explaining the procedure carefully. A single dose of 400 mg. of Miltown or Equanil also serves to relax the patient and allay apprenhension. Other premedication consists of morphine sulfate and scopalomine in the usual preoperative dosages. The radiographic table is covered with a radiolucent sponge rubber mat which makes the patient's position more comfortable. Preliminary films insure proper exposure and provide evidence of a clear intestinal tract. Following the standard preparation of the skin, local anesthesia is carried by infiltration through the muscle layers into the periosteum of the vertebral column. We are convinced that the generous use of local anesthesia is essential.

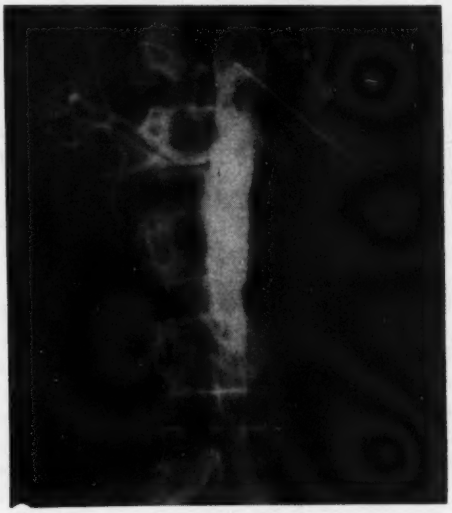
Dr. Colvin H. Agnew and his co-author presented this paper from the Department of Radiology at the University of Texas Medical Branch for the Section on Radiology at the annual session of the Texas Medical Association, April 21, 1959, in San Antonio.

Abdominal aortography is a valuable diagnostic procedure and indispensable in selection of patients for surgery because of occlusive vascular disease of the abdominal aorta and its branches. Knowledge of the principles involved and strict adherence to rules of technique as well as appropriate selection of patients and method permit abdominal aortography with relatively little risk.

The site for introducing the needle as recommended by dos Santos is shown in figure 1C. To puncture the aorta above the celiac axis, the needle is inserted at a 30 degree angle from the verticle just below the last rib and is angled so as to approach the aorta parallel to the twelfth rib. It is directed downward and inward striking the vertebral body. The needle is then withdrawn slightly and the stylet removed, and the tip of the needle is redirected slightly laterally and advanced so that it grazes the anterolateral surface of the vertebral body. With a little practice one soon acquires a sense of resistance that occurs just before the aorta is entered. This is quite helpful because it enables the examiner to thrust the needle inward sufficiently so that the bevel does not straddle the wall of the aorta. When the needle enters the aorta, there is a prompt spurting of blood; but unless there is a considerable hypertension, the blood does not spurt more than about an inch beyond the hub of the 17 gauge needle.



A



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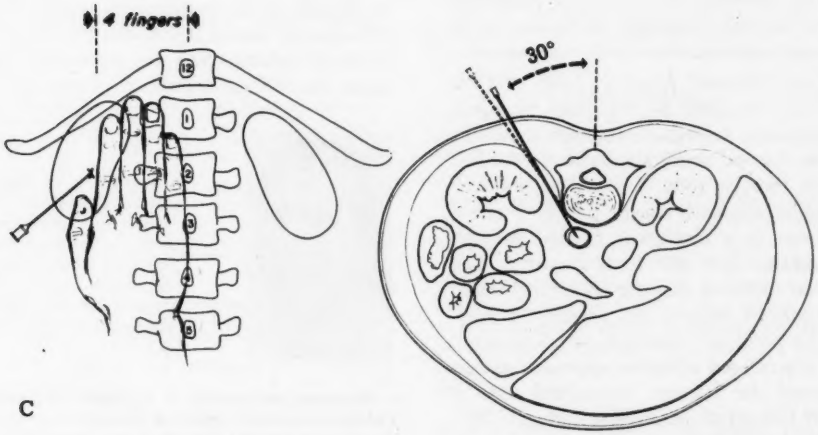

C

Fig. 1A. Front piece from the book by dos Santos and associates published in Paris in 1931.
B. Normal typical translumbar aortogram.
C. Traditional landmarks for the insertion and direction to place the needle above the origin of the celiac axis. To enter below the renal arteries, the direction of the needle should be directed toward the transverse processes of the second lumbar vertebra.

Polyethylene tubing is attached to the needle and both are irrigated at frequent intervals with a 0.002 per cent heparin in isotonic saline solution.

Regardless of the certainty with which the needle is positioned, 5 cc. of contrast substance are injected; and the initial film is exposed, rapidly processed, and viewed. If the needle appears *not* to be clearly within the aortic lumen, it *must* be withdrawn and reinserted at a new level. Although the pulsation of arterial blood in the polyethylene tubing is highly suggestive that the needle tip is within the aorta or one of its major branches, this evidence is unreliable. The length of the bevel of most needles is such that part of the opening may still be within the wall of the aorta or may even be outside. This is illustrated (fig. 3A and E). Figure 3D shows a simultaneous

Fig. 2A. The needle properly placed below the renal arteries for the investigation of aortic and peripheral occlusive vascular disease. There is narrowing of the left external iliac artery.

B. The runoff into the thighs shows the delay produced by the diseased external iliac artery.

C. The demonstration of an unsuspected abdominal aortic aneurysm by the venous angiocardiographic technique.

D. Rather unusual dumbbell-shaped aortic aneurysm arising below the origin of the renal arteries.

E. Complete occlusion of the right common iliac artery with development of substantial collateral circulation.

F. This patient was investigated for hypertension, and a narrow stenotic band with a poststenotic dilatation is demonstrated. This was proved to be due to a congenital stenosis.

injection of both an artery and a vein in which the bevel of the needle apparently lies within both vessels.

Dos Santos recommended that the aortic puncture be made at the level of the twelfth thoracic vertebra. This is well away from the large abdominal branches and yet will provide a satisfactory visualization of the renal arteries. However, if the area of interest is the lower abdominal aorta or the large branches to the thighs and legs, it may be more desirable to place the needle below the renal arteries. The diversion to the kidneys and upper abdominal viscera is thus avoided so that more contrast substance will reach the extremities. When the puncture is made below the renal arteries, the kidneys and intestine would be protected, and probably the spinal cord as well, from the effects of the contrast substance; however, the risk of damage and fatal hemorrhage may be greater since arteriosclerosis is much more common in the distal aorta. Moreover, more frequently than one suspects, the aorta is completely occluded at or just below the renal arteries, and it is impossible to pierce the aorta. Therefore, it has been our recent practice to begin the examination by placing the needle at about the level of the twelfth thoracic or first lumbar vertebra. Following the initial film, the condition of the lower abdominal aorta is determined, and also the nature of the problem which one may encounter may be ascertained more clearly. We believe that there is some merit to the suggestion of Kincaid and Davis[10] that a second puncture can be considered if visualization of the external iliacs, femoral arteries, and other branches to the legs is desired. We occasionally have resorted to a second puncture although generally we try to avoid this.

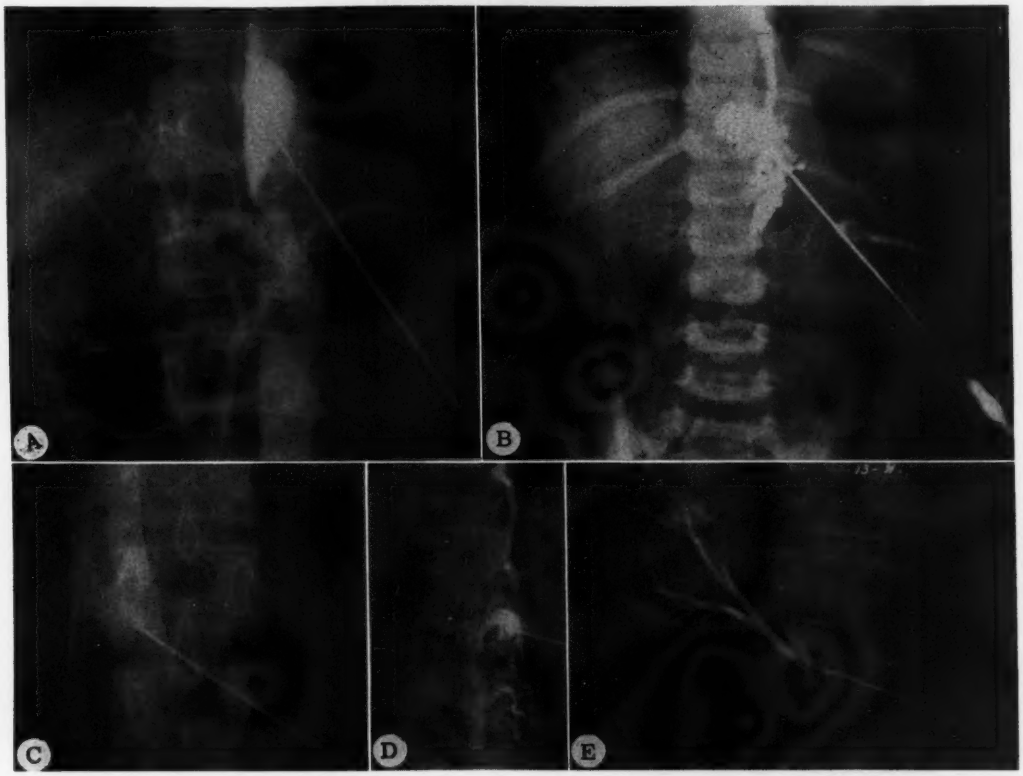

Fig. 3A. A satisfactory aortogram has been produced even though there is para-aortic contrast material and the classic circumscribed oval shadow of an intramural injection.

B. Intramural and para-aortic injection leading to hemorrhage and hemothorax.

C. The minor complication of inadvertent injection of the inferior vena cava.

D. The tip of the needle is in the second lumbar artery with simultaneous injection of the lumbar artery and hemiazygous vein with perilumbar extravasation. The lumbar arteries are well filled providing collateral circulation necessitated by complete aortic occlusion at the bifurcation.

E. The needle lies in the orifice of the right renal artery which divides to supply a kidney with a duplex pelvis and ureter, and there is periarterial injection of contrast material.

Selective Visceral Arteriography.—We prefer selective visceral arteriography when we wish to examine specific branches of the abdominal aorta or when there has been some complication connected with the performance of translumbar aortography. Selective visceral arteriography should not be performed when there is evidence of extensive arteriosclerosis of the lower abdominal aorta or its peripheral branches for fear of dislodging a plaque by manipulation of the catheter. We prefer to expose the artery according to a technique developed by Derrick and his associates.[4] At first, we used a Lehman type intracardiac catheter with a preformed curve. More recently we have had some experience with the catheter described by Ödman,[13] and although our experience has not been extensive, this catheter certainly has definite advantages.

Aortography Using Venous Angiocardiography.—Occasionally we have used venous angiocardiography to advantage in cases of upper abdominal aneurysms when we regard the translumbar approach as dangerous, and we are also reluctant to use a catheter within the abdominal aorta. An example is shown in figure 2C. The technique of this procedure has been widely described before. We hasten to add that the meticulous injection technique is necessary if one is to obtain adequate concentration of the contrast substance in the upper abdominal aorta.

CONTRAST SUBSTANCE

The evolution of iodinated contrast substance since Cameron's preliminary report[2] represents a frequently overlooked technical development. We rarely inject more than 25 cc. of contrast substance, and earlier preferred 70 per cent Urokon because of its high density and low viscosity. However, most patients react with considerable abdominal distress following the injection of this substance. More recently we have been using 85 per cent Cardiografin and 76 per cent Renografin, and the discomfort to the patient has been considerably reduced. The speed of injection may vary according to the portion of the vascular system that it is desired to demonstrate. Demonstration of the renal arteries may be done by the use of 15 cc. of contrast substance injected promptly. Visualization of the lower abdominal aorta and its major branches may be best effected by a somewhat slower injection (5 to 7 seconds) of 25 cc. of 76 per cent Renografin.

FILMING TECHNIQUE

The majority of our examinations are done using the translumber route in which we use a single film under the abdomen and another film under the thigh and lower legs. To compensate for differences in thickness, we have had considerable success using Eastman Royal Blue Film placed in the Bucky tray underneath the abdomen and Standard Blue Brand Film underneath the thighs and upper legs. Another technique that we have explored to some extent is that of using an additional portable machine to film the thighs and lower legs and making this exposure some 2 to 3 seconds after the exposure of the abdominal film. We are still experimenting with other techniques in an effort to demonstrate the entire vascular system from the site of aortic puncture to the ankles.

In the study of renal circulation and also in an effort better to demonstrate the collaterals formed following obstruction of the abdominal aorta, and in nearly all cases of selective arteriography, we have used the Sanchez-Perez or Schonander film changers and exposed film at 1 per second. In general, we try to adapt our filming to the nature of the problem we are studying.

INDICATIONS FOR AORTOGRAPHY

Occlusive Vascular Disease.—A necessary prerequisite for the successful surgical treatment of occlusive disease of the aorta and its branches is a precise knowledge not only of the location and length of the obstruction, but also the vascular system beyond the obstruction. Consequently, occlusive vascular disease is an important indication for aortography. In most instances, we prefer the translumbar route. Every effort should be made by the use of delayed or serial films to demonstrate the entire circulation from the lower abdominal aorta to, at least, the midcalf.

Aneurysms of Abdominal Aorta and Its Branches.—By far the most common site of aneurysm formation is that part of the aorta lying below the renal arteries. Here the diagnosis frequently can be made by the clinical examination and plain films of the abdomen. Since techniques in the use of grafts have improved greatly and since most of these aneurysms do not extend to the level of the renal arteries, it is not essential that all of these cases be subjected to aortography. On the other hand, occasionally there are small aneurysms of the branches of the aorta such as the renal arteries, the hepatic artery, or the external iliac arteries which would remain undiagnosed unless one resorted to aortography. Also occasionally the aneurysm lies partly in the lower thorax and partly in the abdomen in which case thoracic aortography or intravenous angiocardiography would be the procedure of choice.

Vascular Malformations.—Arteriovenous malformations are occasionally encountered and can be

demonstrated by aortography. Recently we demonstrated an arteriovenous communication between the stump of the right renal artery and the inferior vena cava.

Renal Abnormalities.—There is some disagreement as to the accuracy of aortography in the differentiation of renal cysts from malignant tumors. Evans[6] indicated an accuracy of about 95 per cent, whereas Nesbitt implied less confidence and emphasized that even following satisfactory aortography, surgical exploration is resorted to in the majority of cases. Consequently, in our hands, this differentiation is rarely an indication for translumbar aortography.

Aberrant vessels are easily seen by aortography, and sometimes these produce a partial obstruction of the ureter or of the pelvis of the kidney. Alteration of the vascular pattern produced by renal infarcts, hydronephrosis, polycystic disease, and horseshoe and hypoplastic kidneys are sufficiently characteristic to suggest the diagnosis. It is rarely necessary, however, to use this procedure as the diagnosis often can be confirmed by other more easily performed procedures. Selective renal arteriography of the kidney has been of value in the surgical management of renal tuberculosis.[8]

Ever since the demonstration by Goldblatt that unilateral renal ischemia may cause persistent hypertension, clinicians have been looking for conditions which will produce such an ischemia in humans. Abdominal aortography is the logical approach to this problem, and recently we have been impressed by the quality of the demonstration of the vascular bed that can be obtained by selective renal arteriography. This is demonstrated in figures 4D and E. Considerable impetus to these studies has been given by the findings of Poutasse and his associates, who have found bilateral stenosis of the renal artery in many cases associated with hypertension. We have had 2 cases of unilateral renal artery narrowing producing hypertension relieved by vascular surgery. One is shown in figure 2F.

Celiac and Superior Mesenteric Arteriography.—Clinicians have recognized a syndrome characterized by marked weight loss and emaciation, inability to eat normal sized meals without discomfort, and the passage of stools containing excessive amounts of fat and undigested material. This condition often occurs in middle aged persons and has been identified by such terms as abdominal angina or abdominal claudication. Neither term seems to be satisfactory, but the implication is that there is impairment of blood flow to either or both the superior mesenteric artery and celiac arteries. A number of such cases have been reported in the literature[19] in which there was a severe narrowing of the celiac axis or superior mesenteric artery by atheromatous plaques near the origin of these arteries. Selective visceral arteriography is a logical approach to the preoperative study and selection of patients with this condition. Per Ödman has developed a technique for catheterization of these branches. Using a somewhat similar catheter, we have had some success in this connection and have been able already to demonstrate severe narrowing of the superior mesenteric artery in 2 patients. This field is now under active investigation.

Miscellaneous Conditions.—The conditions that may prove susceptible to some modification of abdominal aortography are liver metastasis, carcinoma of the stomach and pancreas, and possibly carcinoma of the colon.

HAZARDS AND COMPLICATIONS

Evans and his colleagues[6] have reported on 2,500 consecutive aortographic studies without a death or serious complication. However, within the past 5 years, sporadic reports of fatalities began to appear in the literature. Recently McAfee[11] has surveyed the experience from numerous and representative institutions in the United States and found that in 13,270 abdominal aortograms, there were 37 fatalities or a mortality rate of 0.28 per cent. In addition, there were 98 serious nonfatal complications (incidence 0.74 per cent). The over-all incidence of fatal or serious nonfatal complications was therefore slightly over 1 per cent. In McAfee's study, renal damage was the most important complication and occurred in about one-third of the fatal cases. Renal damage was distinctly more common in those cases that received a large amount (over 50 cc.) of contrast substance, where the injection was directly into the renal artery, or in those patients with high aortic obstruction. Neurological disturbances consisting of paresthesias and various degrees of paralysis ranging from asthenia to complete paralysis of both lower extremities have been observed. Other fatalities and severe reactions have occurred from a hemorrhage at the puncture site and interference with the blood supply to the intestinal tract. Other causes of death or severe reaction were attributed to anesthesia. Gaylis and Laws[9] clearly demonstrated that intramural injection of isotonic saline in the aortic wall would produce dissection. This preceded shortly a particularly discouraging report from the University of Michigan.[1] Here 3 fatalities were found to have been produced by dissection following the intramural injection of contrast substance. These dissections produced by the intramural injection may be expected to produce the gamut of signs and symptoms exhibited in spontaneous dissection.

A summary of complications observed at the Uni-

versity of Texas Medical Branch in about 160 consecutive examinations is as follows:

1. One case of periaortic injection requiring immediate transfusions and followed by hemothorax requiring eventual decortication (fig. 3B).

2. One case of pneumothorax which required no special treatment (fig. 4B and C).

3. Five cases of intramural injection. There is no record of adverse effects except in 1 patient who temporarily stopped breathing even though there was endotracheal intubation.

4. Six cases of periaortic injection. There was no recorded adverse effect and no special treatment was required.

5. Three cases in which one of the major branches of the aorta was injected. No adverse effect was recorded and no treatment was required.

6. One case of acute thrombosis at the site of insertion of the catheter in the femoral artery. Signs and symptoms developed 12 hours following selective visceral aortography. The thrombus was removed promptly without any disability.

PROPHYLAXIS

By far the most important prophylactic measure is to have the procedure performed by those who are aware of the proper indications and possible complications, who observe the most meticulous technique in puncture and catheterization, and who have the poise and judgment to discourage its ill-advised use. However, adherence to the following directives will reduce the risk of the procedure. Evans[6] has advocated stricter rules.

Fig. 4A. In a complete situs inversus the patient was wisely approached from the right side.

B. In a markedly emphysematous person, the usual placement of the needle pierced lung, producing the pneumothorax demonstrated in **C.**

D. Inadvertent injection of the right renal artery demonstrating selective visceral arteriography by the translumbar method.

E. Catheter threaded into the right renal artery demonstrates the excellent anatomic detail without superimposed irrelevant vessels.

1. Several attempts to puncture the aorta at the same site should *never* be undertaken.

2. A single film should be taken following the injection of only 5 cc. to determine accurately the position of the needle. If there is any doubt as to the location of the needle, it should be withdrawn and reinserted at a different level.

3. The volume of contrast material should be limited to 20 cc. above the renal arteries. When there is a complete block of the aorta below the renal arteries, advantage should be taken of delayed filming to visualize collateral circulation rather than increasing the amount of contrast substance.

4. Tranquilizers and local anesthesia should replace general anesthesia. It appears that physicians are more considerate of patients under these circumstances and that there is the further advantage of minimizing the risk of anesthesia.

5. Serious consideration should be given to limiting the total amount of contrast material injected during one procedure to 60 cc. although we have given as much as 100 cc. with repeated injections. It is probably safer to repeat the procedure than to employ larger amounts of contrast substance.

6. Selective visceral arteriography via the femoral artery should not be undertaken in the presence of moderately advanced femoral arteriosclerosis. It may not be detected until the artery is exposed. Even then, it is probably safer to withdraw and use another method.

7. All patients should be observed in the hospital for 24 hours after examination.

CONCLUSION

Abdominal aortography is a valuable diagnostic procedure and is indispensable to the surgical selection of those patients with occlusive vascular disease of the abdominal aorta and its branches. There are no absolute contraindications with the possible exception of hypersensitivity to iodine. It may not be necessary in the demonstration of abdominal aneurysms, but it is certainly helpful in establishing the limits, origin, and ramifications of arteriovenous fistulas and congenital malformations of the aorta and its branches. Safe lumbar aortography is influenced by knowledge of the principles involved and is entirely dependent upon the strict rules of technique. With the appropriate selection of patients and method, abdominal aortography can be performed with relatively little risk.

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Dr. Agnew, Kansas University Medical Center, Department of Radiology, Kansas City, Kan.

Dr. Cooley, Department of Radiology, University of Texas Medical Branch, Galveston.

Older People Tend to Have Low Protein Diets, Says VA

People over 50 have a tendency to select diets low in essential protein needed to maintain health and vigor, Veterans Administration research indicates.

Older people apparently have a greater requirement for the essential amino acids, protein constituents found largely in eggs, meat, and milk, than do younger people, said Dr. Stewart G. Tuttle, spokesman for a research team at the Los Angeles Veterans Administration center. Yet the team's study indicates people over 50 tend to select diets that are low in these essential amino acids, Dr. Tuttle said.

"Our study suggests that lack of the essential amino acids may cause a nutritional imbalance in older people that makes them more susceptible to development of degenerative diseases and speeds the aging process," said Dr. Tuttle.

Surgical Emergencies In Pregnancy

NEWELL W. PHILPOTT, M.D.

Montreal, Canada

COMMONPLACE surgical problems become, at times, of alarming import when they occur during pregnancy. This is of great significance because several authorities have shown that the incidence of acute appendicitis, gallbladder disease, and other lesions of the gastrointestinal tract is as great in the pregnant as in the nonpregnant female population.[3]

Many mistakes have been made in the handling of these conditions which required active surgical intervention during pregnancy. The errors in management were usually due to incomplete medical investigation or may be attributed to errors in judgment. These deficiencies not infrequently have been due to the fact that the operator was a surgeon who lacked knowledge of the manifestations of these conditions during pregnancy. Perhaps, more frequently it has been relative to the fact that an obstetrician was in charge and that he has had insufficient experience in the handling of those acute surgical lesions which lie outside the realm of ordinary obstetrical practice.

These facts emphasize the importance of adequate training for any surgeon who is permitted to open the abdomen. In addition, the general surgeon and the obstetrician should be urged to become more familiar with the manifestations of general surgical conditions which may be encountered in obstetrical practice.

It is my intention to present findings of those more common surgical problems which are observed in a large obstetrical center. Extraordinary entities purposely will be omitted. For example, Kobak and Hurwitz of the University of Illinois have reviewed 31 cases of perforation of the pregnant uterus by gunshot wounds.[4] In Montreal we have no knowledge of this type of mishap, and I shall refer only to those conditions which are seen with some frequency in our institution.

Barter and Rovner of Washington reported all extrauterine complications which were treated by operation in a 5 year period.[1] There were 45,720 deliveries, and only 41 patients had an operation of this nature.

Mendenhall reviewed the cases of acute appendicitis complicating pregnancy which occurred in Sloane Hospital, New York, from 1934 to 1957.[5] Only 19 women manifested definite proof of acute appendicitis. This was an incidence of 0.026 per cent.

In supplementing a report of 10 years ago by a careful study of all cases during the last 2 years at the Royal Victoria Hospital I found a much higher incidence of surgical intervention during pregnancy. Though the number of patients in the last 2 years is too small to be statistically significant the findings are of sufficient interest to be presented.

The report of the 1957-1958 period involves 7,372 obstetrical patients. There were only 2 maternal deaths, and the fetal mortality, all types included, was 2.4 per cent.

Included in this total were 55 patients who had extraordinary surgical procedures during pregnancy or at the time of delivery. In this select group no mothers were lost, but the fetal deaths were 9.

Dr. Newell W. Philpott, professor of obstetrics and gynecology at McGill University Faculty of Medicine, presented this paper for the Section on Obstetrics and Gynecology at the annual session of the Texas Medical Association in San Antonio, April 21, 1959.

Commonplace surgical problems occurring during pregnancy may have alarming import unless handled carefully. Of 7,372 obstetrical patients, 55 required extraordinary surgical procedures during pregnancy or at delivery. The general surgeon and the obstetrician should become familiar with manifestations of conditions which complicate pregnancy but are not encountered frequently in ordinary practice.

There has been an exclusion of all types of uncomplicated cesarean sections. Other deletions are conditions such as tubal pregnancies and the various procedures for incomplete and inevitable abortion. However it should be stated that our gynecological service admitted 4,953 individuals in this 1957-1958 period. There were 41 tubal pregnancies and 870 various forms of abortion, an incidence of 18 per cent of the total gynecological admissions. No mortality occurred in this group.

The 55 patients who experienced extraordinary surgical procedures should be presented in detail. For the sake of brevity they have been grouped as follows: (1) extragenital abdominal lesions, (2) surgical conditions occurring in the abdomen and associated with the genital tract, and (3) other less common types of surgical procedures which occurred during pregnancy.

EXTRAGENITAL ABDOMINAL LESIONS

Acute appendicitis which occurs during pregnancy is of established interest. The experience of any hospital service relative to acute appendicitis is necessarily limited by the infrequent association of the two conditions. Most authors agree that pregnancy does not predispose to appendicitis; it would appear that appendicitis and pregnancy may coexist with little alteration of either condition.

During the last 2 years a laparotomy was performed on 18 individuals with the preoperative diagnosis being of an extragenital nature. It is interesting to note that in 12 instances the preoperative diagnosis was definite or probable acute appendicitis complicating pregnancy. The final diagnosis showed acute appendicitis in 5 patients, questionable chronic appendicitis in 2, volvulus with obstruction in 1 instance; twice degenerated fibroids were the cause of the acute symptoms; on 1 occasion there was a twisted right sided ovarian cyst; and no pathological lesion was found in 1 patient.

TABLE 1.—*Laparotomy for Extragenital Lesions During Pregnancy, 1957-1958*

Lesion		No.
Appendicitis		7
Acute	5	
Chronic	2	
Cholelithiasis		3
No lesion found		1
Bands of adhesions		1
Volvulus & obstruction		1
Neoplasm of sigmoid		1
Total		14

Table 1 lists the diagnoses for the extragenital lesions. It should be noted that there were 3 cases of cholecystectomy, all performed between the third and sixth months of pregnancy. The other surgical conditions were treated at various stages of the pregnancy.

ASSOCIATED GENITAL LESIONS

Two conditions which are primarily gynecological and which frequently complicate pregnancy are uterine fibromyomas and ovarian cysts (table 2). Management of these conditions plays an important role in the eventual result.

In a previous study our records showed that fibromyomas of the uterus occurred much more frequently than unilateral and bilateral ovarian cysts.[6] In 15,949 obstetrical cases there were 211 fibromyomas complicating pregnancy and 24 unilateral or bilateral ovarian cysts in the series.

The method of treatment for the obstetrical patient with fibroids varies considerably from that used when an ovarian cyst is the complicating factor. When fibroids are present, management should be of an expectant nature. Progress of a normal pregnancy and delivery should not be made abnormal by some meddlesome obstetrician. Only when the patient experiences repeated attacks of acute pain, vomiting, or fever should myomectomy be considered during the pregnancy. Adequate sedation and bed rest are invaluable for the relief of pain and the prevention of subsequent attacks. At our hospital we believe that repeated doses of morphine or some similar drug are most efficacious. We do not administer progesterone or estrogens as a routine measure because there is rarely a deficiency found in this type of case.

TABLE 2.—*Laparotomy for Genital Conditions During Pregnancy, 1957-1958.*

Condition	No.
Twisted ovarian cyst	4
Myomectomy	5
SURGERY AND CESAREAN SECTION	
Removal of ovarian cyst	2
Hysterectomy (fibroids)	4
Myomectomy	6
Abdominal pregnancy	1
Total	22

Delivery per vaginum may be carried out in the presence of fibroids provided there is no obstruction offered the fetus in the birth canal. Because of the possibility of degeneration in the postpartum involuting period, removal of larger fibroids should be considered and such removal can be accomplished toward term by means of a cesarean operation.

Our treatment of 211 obstetrical patients with fibroids was as follows: cesarean section with hysterectomy was performed in 29 cases; myomectomy with cesarean section in 24 cases; myomectomy during pregnancy in 16 cases; and delivery per vaginum in 156 cases.

If a myomectomy is indicated during the pregnancy, most authorities agree that whenever it is possible it should be performed after the ninetieth day of pregnancy. The uterus is less irritable and placental function is well established by this time. We follow the rule that a cesarean section should be the method of delivery following those cases of myomectomy in which the fibroids are intramural. When they are situated subserous or are pedunculated, delivery per vaginum is recommended.

One may ask if it is necessary to do a cesarean section at any time following myomectomy. Accidents do occur. One of our patients had a myomectomy for intramural fibroids. Three years later when the patient was 8 months pregnant she was seized with a sudden sharp pain which was followed by profound shock. A cesarean operation was performed 2 hours later at which time a rupture of the old scar 5 cm. in length was found accompanied by massive intra-abdominal hemorrhage, and the baby was delivered dead. Fortunately the mother survived.

When there is an ovarian cyst of any appreciable size—6 cm. in diameter or larger—and the patient has an intrauterine pregnancy, she should be treated somewhat differently. Complications are prone to occur due to twists in the pedicle with consequent impairment of circulation in the predelivery or postdelivery state. Obstruction to labor is not infrequent. Some authors suggest removal of all ovarian cysts at around 12 weeks of pregnancy. We agree that if there is a suggestion of any such complication, operation is indicated. Of the 24 cases which were diagnosed during the 5 year period 12 patients came to operation at some time during the pregnancy.

It is essential to diagnose these cases in early pregnancy because they are difficult to detect in later months. They may be inaccurately diagnosed as fibroids of the uterus. By pelvic examination in the first 3 months of pregnancy an accurate diagnosis usually can be made. Roentgen examination is an aid in this type of case because approximately 50 per cent of cysts which occur in pregnancy are dermoid in origin, and they usually contain radiopaque material.

There were 4 persons in whose cases both ovaries were removed because of the presence of large bilateral dermoid cysts. Two of these patients were operated upon before 90 days' gestation. Most certainly it is important that these patients be given sedation during the preoperative and postoperative period.

In addition, if there is any indication that the corpus luteum has been removed along with the cyst, these patients are benefited by large doses of progesterone and estrogenic substances. We prefer the intramuscular administration of progesterone in amounts not less than 50 mg. per day. This may be used in conjunction with the oral administration of diethylstilbestrol.

Dangers of abortion after 90 days of pregnancy are not great. The placental function is well established and progesterone production is carried on by the placenta.[2]

MISCELLANEOUS CONDITIONS

The other more unusual surgical conditions are noted in table 3.

TABLE 3.—*Other Conditions Requiring Surgery During Pregnancy, 1957-1958.*

Condition	No.
Bartholin cysts	5
Removal of renal calculi	3
Major orthopedic surgery	3
Radical mastectomy	2
Removal of breast nodule	2
Heart surgery	2
Simple mastectomy	1
Excision of cancer of labia	1
Total	19

Suffice it to remark that all these various conditions were treated with definite benefit to the mothers though there was added risk to the fetal outcome.

It should be noted that one abdominal pregnancy is included in the list. This case may be of sufficient interest to describe in detail.

CASE REPORT

Mrs. V., aged 37, had been married 14 years. There had been extensive sterility investigation and various therapeutic measures. Hospitalized on three occasions during pregnancy for severe abdominal cramps, backache, and weakness, she was treated with large doses of progesterone and sedatives. A septate type of uterus was considered possible, with two separate masses being palpated in the abdomen. It was decided to contemplate a cesarean delivery.

Last admission occurred 6 weeks before term with the patient having suspected labor pains and a showing of blood. She received more progesterone and repeated sedation. Three days later there was profuse uterine bleeding followed by the passing of a decidual cast. One day later a laparotomy was performed and an abdominal pregnancy was found. The sac and placenta were attached to the omentum, transverse colon, several loops of ileum, and the parietal peritoneum of the pouch of Douglas. A live baby of 2,160 Gm. was delivered. Even with extreme care some maternal sinuses were torn and devastating hemorrhage occurred. The cord was cut short and the placenta was left intact in the abdominal cavity. The abdomen was closed with no drain being used. Profound shock was treated with 14 pints of blood over a 48 hour period.

The fetal sac filled with blood and bowel obstruction symptoms were marked for 22 days; this necessitated a Levin tube and careful electrolyte control. A posterior colpotomy and drainage of 2,000 cc. of purulent bloody fluid were performed. This was followed immediately by marked improvement for 3 weeks.

Two days after the patient's figured due date (January 24, 1959) there was separation of several cotyledons of placenta; repeated severe hemorrhages from the colpotomy wound occurred over the next 8 days. This was controlled by tight packing and the liberal use of whole blood.

Three months following delivery the mother and baby

are progressing favorably. It should be stated that 49 pints of blood were used during the total postpartum period.

SUMMARY

Various conditions requiring active surgical intervention may occur during pregnancy. These should be treated when definitely diagnosed. The general surgeon and the obstetrician should be stimulated to become more familiar with the manifestations of those conditions which complicate pregnancy but which are not encountered frequently in ordinary practice.

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Dr. Philpott, Department of Obstetrics and Gynecology, McGill University Faculty of Medicine, Montreal, Canada.

Less Premedical Training Recommended by Physicians

How medical education looks today both to medical students and practicing physicians was the theme of the nationwide survey reported in the November issue of *Patterns of Disease*, a publication distributed by Parke, Davis and Company. The survey was conducted among 9,862 medical students representing 51 of the nation's 84 medical schools and 5,065 physicians.

A major point of student-physician disagreement concerned premedical preparation for medical school. Practically all of the students received undergraduate degrees, with only 11 per cent having no degree. Approximately 80 per cent of the medical students felt their premedical education to be valuable preparation for medical school, giving as their major reason background broadened in nonscientific areas. Close to half of the physicians, on the other hand, felt that a 4 year premedical education was not necessary for medical studies. Most frequently cited reason was a "shorter period would be adequate."

However, both students and physicians favored more emphasis on liberal arts than on science. Close to 85 per cent of the students had majored in science, but only about 20 per cent said that they would now recommend heavy science programs. About 40 per cent of the physicians felt that premedical education should stress liberal arts, with approximately 30 per cent preferring basic sciences.

Elective Induction Of Labor

J. L. JACKSON, M.D.

Wichita Falls, Texas

FOR MANY YEARS midwives, physicians, and later obstetricians have adhered to the axiom of "leave her alone long enough and she will deliver her baby herself." With the removal of the majority of the natural hazards to the parturient by modern scientific obstetrics, the patient and physician have turned their attention to the alleviation of discomforts endured by the expectant mother. Much attention has been given to sedatives and anesthesia during labor, but little has been done to aid the awkward and uncomfortable patient in the latter weeks of gestation. More recently, the pharmaceutical companies have turned their attention to a large list of sedative drugs and are urging their use to promote sleep and relieve the discomfort during the waning days of pregnancy.

Induction of labor has long been reserved for the severe toxemia, hypertension, or other complications of pregnancy. Disagreement continues in professional circles regarding the early induction of labor for the Rh sensitized patient. For many years, labor has been induced by the use of castor oil, quinine, enemas, and their various combinations. Already belonging to antiquity is the Voorhees bag. In more recent years, various Pituitrin products have been employed to induce labor. More recently, Pitocin has been employed intravenously, with the results ranging from glowing success in all cases to outright condemnation of the whole procedure. Surely time will bring the results of Pituitrin induced labor to a reasonable level and add it to our growing armamentarium of useful and accepted procedures.

This paper deals with a simple and extremely easy procedure for the induction of labor. For many years, obstetricians have employed the simple rupture of membranes as treatment for eclampsia and preeclampsia. Many patients, so treated, were found to go immediately into labor and to deliver in a relatively short time.

Several years ago, I became interested in attempts to determine the relationship of the cervix to the expected interval before the onset of labor. Very cautiously, and with exceptional care for as nearly an aseptic technique as possible, I began routinely to make pelvic examinations on each patient as she visited the office during the last 2 or 3 weeks of

pregnancy. Over a period of time, I found that I could become fairly accurate in my predictions as to the onset of labor. Somewhere, I acquired the now commonly used term, "ripe cervix."

From this cautious beginning, a more brazen attitude was taken until today; every patient is examined vaginally at each office visit, beginning 3 weeks prior to the expected date of confinement. No special techniques are employed. The surgically clean, but nonsterile glove, employed in any vaginal examination, is utilized along with an ordinary surgical lubricant. As the statistics point out, no interuterine infections have resulted.

RIPE CERVIX

The "ripe cervix" is difficult to describe. The usual relationship of the lower uterine segment to the cervix is altered, so that the internal os becomes obliterated and the cervical canal is shortened. The external os becomes slightly dilated, and the remaining cervix is softened and becomes distensible. The ability accurately to recognize the ripe cervix is not easy. Attempts to teach the technique to resident physicians have been disappointing.

Dr. J. L. Jackson of Wichita Falls presented this paper at the Texas Medical Association's 1959 annual session before the Section on Obstetrics and Gynecology, April 20 in San Antonio.

Elective induction of labor by simple rupture of the membranes for a patient with a ripe cervix is a safe procedure, well accepted by patients. It eliminates some of the discomforts of the latter days of pregnancy and shortens the length of labor.

As the expected date of confinement approaches, the head becomes fixed lower in the pelvis, and the cervix becomes progressively shorter. As the cervix shortens to the point where it is almost flush with the lower uterine segment, it becomes extremely soft. The os begins to open and would permit the introduction of a finger of the examining hand. There is no constant relationship between the expected date of confinement and the time of the ripening of the cervix. However, in most cases, the cervix will be ripe about 7 to 10 days before the expected date of confinement. By this time, the patient is complaining of constant pressure, extreme frequency of urination, difficult walking, inability to sleep, and in a continuing state of discomfort. These would be described simply as the discomforts expected in the latter part of pregnancy, and it would be expected that labor would ensue in a few days. Loss of sleep is common, and the fatigue which results produces anything but a relaxed patient, well prepared for labor.

When it has been determined that the cervix is ripe, the patient is so advised and surgical induction of labor is offered to her. She then is admitted to the hospital and prepared in the usual manner. A sterile vaginal examination is made, using pHisoHex as a lubricant. With two fingers of the examining hand in the vagina, the cervical os is felt. One finger is inserted into the cervix and the membranes are gently stripped from the lower uterine segment. This usually increases the amount of the forewater. The second finger is introduced into the cervix, if possible, and a long Allis hemostat is inserted between the fingers. A slight twisting motion will rupture the bag and allow the drainage of the forewater. One or both fingers are then introduced into the rent into the amniotic sac, enlarging it sufficiently to allow free escape of the amniotic fluid. Care is exercised to allow the fluid to escape slowly as possible and to prevent the displacement of the head. A uterine contraction usually follows in 30 to 60 seconds, and the hand is then withdrawn. The fetal heart sounds are carefully noted and the patient is instructed to remain in bed. The average patient will begin active contractions within 15 to 45 minutes, and labor will ensue at a moderately rapid pace. More experience has suggested that the riper the cervix, the more quickly is the onset of labor.

EVALUATION OF PROCEDURE

From my private practice, 1,418 cases have been reviewed. Of these, 249 cases have been eliminated for the following reasons: 98 cesarean sections; 24 unable to determine the length of labor (it is noted that these occurred during the early years, when records were not as accurately kept as they are today); 41 breech presentations; 9 sets of twins; 1 eclampsia; 39 premature labors (resulting in the delivery of very small infants, some of which were previable); 1 prolapsed arm; 1 large meningocele; 1 cervical dystocia (due to a previous surgical procedure); 1 transverse lie; and 15 prolonged labors due to small pelves.

A total of 743 normal labors in patients with cephalic presentations were used as a control series. Approximately 410 cases constitute the series of elective inductions of labor. Sixteen cases where elective induction of labor was instituted have been eliminated for the following causes: 2 inductions performed for toxemia, upon cervices that were not

considered ripe by the usual definition; 6 cases in which intravenous Pitocin was employed; 2 cases of prolonged labor, due to a platypelloid pelvis; 3 cases of prolonged labor, due to a small pelvis; 1 case of amnionitis (present at the time of induction); and 2 cases of primary inertia.

The 1 case of amnionitis is not easily explained. The patient was selected for an elective induction of labor and admitted to the hospital. When the membranes were ruptured, there was a foul odor to the amniotic fluid. The subsequent labor was somewhat prolonged, but fortunately, a viable fetus resulted, and there were no further maternal complications. The 2 cases of dystocia must be considered failures of the elective induction of labor procedure. One was on a physician's wife, who gave a history of previous prolonged labors. The membranes were ruptured in the usual manner and labor did not ensue. Delivery was finally accomplished after various Pituitrin procedures and a rather prolonged labor. The other case is an outright failure of the procedure. In that, the patient had had a previous cauterization of the cervix which was believed not to have altered the cervix, and the cervix was considered ripe at the time of induction. However, after the rupture of membranes, labor did not ensue and delivery was not accomplished for more than 24 hours.

TABLE 1.—*Average Time in Labor for Spontaneous and Induced Labors.*

Year	Noninduction Cases	Noninduction Av. Time (hr.:min.)	Induction Cases	Induction Av. Time (hr.:min.)
1951	17	7:47		
1952	120	8:20	60	4:03
1953	139	8:32	63	4:32
1954	127	9:47	48	5:37
1955	121	9:32	61	4:49
1956	62	9:49	69	4:57
1957	76	9:58	54	5:15
1958	83	10:15	55	5:58
Total	745	9:19	410	4:59

TABLE 2.—*Percentage Distribution of Time in Labor for Spontaneous and Induced Labors.*

Hr. in Labor	Noninduction No.	Noninduction %		Induction No.	Induction %	
< 2	55	7.6	31	51	13	62
2 - 3	50	7		72	18	
3 - 4	54	75		74	19	
4 - 5	68	9.4		64	12	
5 - 6	74	10	55	35	9	84
6 - 7	65	9		38	9	
7 - 8	37	5		20	5	
8 - 9	42	6		12	3	
9 - 10	38	5.2		9	2	
10 - 20	209	29		35	9	
20 - 30	53	7.3		0	0	

Table 1 shows the average length of time in labor for 743 normal deliveries, with a spontaneous onset of labor. The time in labor was determined as that interval of time elapsing between the onset of regular contractions and the end of the second stage of labor. It will be noted that this series is taken from deliveries from 1951 through 1958. All prolonged labors have been excluded as noted in table 1. The average length of time in labor was 9 hours and 19 minutes. The table also shows the evaluation of 410 electively induced labors, between the years 1952 and 1958. The time in labor, for these electively induced labors, was that time from the artificial rupture of the membranes to the completion of the second stage of labor. This eliminates any margin of error due to the lag in time between the rupture of the membrane and the time of the onset of labor, which might be difficult to determine. The average time for these 410 induced labors was 4 minutes 59 seconds. It is interesting to note that after eliminating all abnormal labors, the electively induced patient was in labor approximately one-half the time of the patient whose labor was of a spontaneous onset.

Further evaluation of the length of time in labor (table 2) reveals that in the induction group, 31 per cent of the patients had delivered within 3 hours after the rupture of the membranes. In the control series, it was 5 hours before 31 per cent of the patients had delivered. By the end of 5 hours, 62 per cent of the induced group had delivered. By the end of 8 hours only 55 per cent of the noninduced group had delivered whereas 84 per cent of the induced group had been delivered within this period of time. Only 9 per cent of the induced patients took more than 10 hours to deliver whereas in the noninduced group, 36 per cent of the patients failed to deliver within the first 10 hours of labor.

Since delivery procedure might conceivably alter these figures, the types of delivery for each section is evaluated and noted in table 3. Of the 743 control cases, 112 were delivered spontaneously and 631 by elective low forceps. Thus, it is noted that approximately 85 per cent of the control series was delivered by elective low forceps. In the electively induced group of 410, 28 were delivered spontaneously and 362 by elective low forceps. This constitutes 95 per cent of this series and might conceivably somewhat alter the average length of time in labor, but not to a great degree. In accumulating these fig-

TABLE 3.—*Types of Delivery for Spontaneous and Induced Labors.*

	Total	Spontaneous	Low Forceps	General Anesthetic	Saddle Block Anesthetic
Noninduction	743	112	631	221	522
Induction	410	28	382	61	349

ures, it was noted that the majority of the spontaneous deliveries occurred earlier in practice and were naturally found in a higher degree of multiparity. In the control group, 221 were delivered under general anesthesia and 552 under saddle block anesthesia. This does not compare quite so favorably with 61 general anesthetics and 349 saddle blocks of the 410 electively induced labors. Again in compiling these statistics, it was noted that a saddle block anesthesia was used much more frequently in recent years.

No figures are shown as to parity of these patients. However, the majority of the patients are relatively low parity, as usually noted in the private obstetrical practice. It is thought that the spread between primipara and multipara was approximately equal between the two groups.

Infant morbidity figures are not readily available for either of these groups. However, I am unable to recall any serious morbidities that might in any way be considered the result of the elective induction of labor. As noted earlier, premature infants have been excluded from this series. After the elimination of congenital abnormalities, only 4 infant mortalities are recorded for the two series. Three infant mortalities occurred in the control series, 1 of which was eliminated because of a breech position which resulted in a stillborn infant. A second patient was delivered by emergency mid forceps in 1952, after severe fetal distress was noted. The cord was found wrapped tightly around the neck five times and the infant could not be revived. The third case involved an Rh sensitized mother who had an erythroblastotic baby. The child survived exchange transfusion, only to succumb to the disease in approximately 6 weeks. Only 1 case in the electively induced labors resulted in an infant mortality. The infant was delivered after an uncomplicated labor which was within the limits of the averages for the induction of labor. The child was somewhat sluggish at the time of delivery, but its cry was considered good and it was placed in the nursery. Approximately 6 hours later, the child became cyanotic and the pediatrician in charge of the case made a diagnosis of congenital heart disease. In approximately 48 hours, the infant succumbed, and the postmortum examination revealed congenital atelectasis, with poorly expanded lungs, bilaterally, and increased amount of fibrin tissue with the unexpanded portions of the lung. Although it is conceivable that this mortality might in some way be connected with induction of labor, I believe after seeing similar cases under other circumstances that it is unjust to attribute this infant mortality to the induction of labor.

It has long been the opinion of the laity that induction of labor resulted in a longer labor than if labor was allowed to start spontaneously. It also has been long noted by the laity that a dry labor was a longer and more difficult labor. It has been necessary to overcome these attitudes as elective induction of labor has been "sold" to the patient and her family. With its beginning use, elective induction was used more for convenience of patient, physician, and hospital. However, the longer the procedure was employed, the more obvious it became that the average length of time in labor was decreased by the elective induction of labor. The only conclusion which can be drawn is that in years past induction of labor has been employed primarily upon the complicated case and, therefore, the prolonged labor might be anticipated. Certainly it is without foundation that the loss of amniotic fluid results in a prolonged and "dry" labor.

Explanations of these results have not been entirely obvious, but some definite conclusions have been noted. For a long time it has been believed that the anxious, upset patient was in labor longer than her calm sister. It, therefore, has been concluded that the patient who has been allowed to enter the hospital at an appointed time in a calm state and given an adequate amount of time to arrange her household, locate her husband, and wait calmly for a short period of time before the onset of labor is in a much better mental state than the patient who suddenly finds herself in labor with a household to be disposed of, a husband to be found, and perhaps an unnecessarily rushed trip to the hospital. In observing these induced patients in labor, it has been my opinion that the patients do not ask for sedation quite as early as their sisters who have experienced a spontaneous onset of labor. Cervical dilatation is more rapid, less pain is noted, and the patient, therefore, is ready for delivery after a short interval of time.

In relation to table 2 there is some additional information which is interesting to note. There is no reason to explain the increasing average of time in labor for the control series unless it might be a more accurate evaluation of the time in labor due to an increased interest on the part of the nursing personnel to determine accurately the time in labor as this study has progressed. It is thought that the slight increase in time in labor in the induced series is due to my eagerness to utilize the procedure and, therefore, it has been employed where the cervix is not quite as ripe as in the early days of the series.

CONCLUSIONS

From the review of these 1,418 cases taken from private practice, it is concluded that:

1. Elective induction of labor by simple rupture of the membranes is a simple and safe procedure.
2. The evaluation of the ripe cervix is considered extremely important.

3. Elective induction of labor is not applicable to 100 per cent of the cases, but as skill with its use increases, it can be applied to approximately 50 per cent of the patients approaching expected date of confinement.

4. There is no apparent increased infant morbidity or mortality.

5. This is a procedure which has gained wide acceptance by patients because of the relief of the disturbing discomforts of the latter days of pregnancy. It is particularly well accepted by the multiparous patient, who finds that planned labor is less disturbing to her household than the spontaneous onset of labor at an inopportune time.

6. It adds convenience to the obstetrician and to the hospital by allowing induction of labor at an optional time.

7. It shortens the time in labor.

It may be said that elective induction of labor by simple rupture of the membranes for a patient with a ripe cervix is a completely safe procedure, well accepted by the patient. It eliminates some of the discomforts of the latter days of pregnancy by terminating the pregnancy at a time when its continuation does not produce beneficial effects for the mother or the infant. Elective induction of labor upon a patient with a ripe cervix actually shortens the length of time in labor, thereby decreasing the amount of trauma to the baby and discomfort to the mother.

Dr. Jackson, 1314 Ninth Street, Wichita Falls.

ABSTRACT OF DISCUSSION

DR. E. T. COATES, San Antonio: Dr. Jackson is to be congratulated on his paper on this still controversial subject. His emphasis on the "ripe cervix" is well taken. The evaluation of the ripe cervix is of the utmost importance, and one will find that any adverse experiences in the induction of labor are usually due to a misinterpretation of this one factor. One cannot rely on a rectal examination.

The point of not using any oxytocics is interesting, because in our inductions we have found that frequently the cervix which appears to be "ripe" will become firm and even re-form under the stimulation of oxytocics.

The one drawback to elective induction is that the physician must accept a certain amount of additional responsibility even though any adverse happening might have occurred in a spontaneous labor. Another situation that one has to guard against is the patient who is so desirous of having her labor induced that she brings pressure to bear on the obstetrician to induce labor before the findings are favorable, especially in instances in which labor has not occurred by the time of the expected date of confinement.

Experience with Cervical Cytology In a Clinic Practice

W. T. KABLE, JR., M.D.;
E. S. IRVINE, M.D.; and
E. W. IRVINE, JR., M.D.

Wichita Falls, Texas

THE DETECTION of carcinoma of the cervix has undergone considerable change since Papanicolaou and Trout[1] put cervical cytology on a sound basis in 1943. Twenty years ago a clinician felt fortunate to find carcinoma of the cervix limited to stage I. If cervical cytology is included in the annual examination of cancer free women, invasive carcinoma of the cervix may be prevented.

Each of us has a responsibility in cancer detection. A history, physical, and pelvic examination with visualization of the cervix is no longer an adequate means in ruling out carcinoma of the cervix. In the past, with the exception of those coming to the gynecological department, Papanicolaou smears were not done routinely on all new patients coming to our clinic. We now plan for them to be routine on all new patients in the medical, surgical, obstetrical, and gynecological departments.

METHOD

Various collection techniques are designed to obtain cells exfoliated from the lining of the reproductive tract. In the current study, material for cytologic examination was obtained from women who had not douched in the previous 24 hours. An unlubricated speculum was inserted, and material was obtained by aspiration of the posterior fornix and by scraping the squamocolumnar junction. This material was smeared on slides and immediately immersed in equal parts of 95 per cent ethyl alcohol and ether. The slides were stained by a modification of the Papanicolaou method. The slides were read by pathologists in practice in our community. The usual cytological criteria for determining malignancy were applied.

Recent studies by Berg and Bader have shown that the cervical mucous plug contains most of the exfoliated cancer cells. Cells from the squamocolumnar junction are necessary for a high degree of ac-

curacy in the diagnosis of early carcinoma of the cervix. Smears taken from only the posterior fornix result in a higher number of false negatives. A greater number of false negatives also will result when smears are taken from the external cervical os after the mucous plug has been removed.

In the future, two tools will be used by us: (1) a cotton swab for deeper penetration of the cervical canal (90 per cent of cervical carcinomas spread upwards toward the uterine cavity rather than out to the portio); (2) an Ayre type spatula to scrape the squamocolumnar junction.

RESULTS

During the 3 years 1956 through 1958, a total of 1,565 smears were made. Three carcinomas of the cervix were found during this interval; 2 were carcinoma in situ, and the third was a stage I squamous cell carcinoma of the cervix. These 3 carcinomas made the detection rate 1.9 carcinomas per 1,000 smears. The 2 carcinomas in situ were in patients without any symptoms referable to the pelvis. The invasive lesion was in a postmenopausal woman who had had some spotting for several months. The cervix in this case was described as having an erosion on the anterior and posterior lips. The cervices of the patients with in situ lesions showed lacerations and erosions about the external os. Thus, all cervices in this series showed abnormalities, although only in the invasive lesion were any symptoms present.

There were 6 smears reported as positive for cancer cells in which the diagnosis of cancer was not made. Follow-up on 1 patient was not obtained. Atypical hyperplasia of the cervical epithelium was the pathological diagnosis in 3 of the remaining 5 cases. One case showed endometrial hyperplasia, and the remaining 1 showed extensive chronic inflammation. Thus, even though these patients did not present carcinoma, they did present lesions that needed treatment.

Dr. W. T. Kable, Jr., and his co-authors, physicians at the Wichita Falls Clinic-Hospital (Dr. Kable) and Bethania Hospital (co-authors), presented this paper for the Section on Obstetrics and Gynecology at the Texas Medical Association annual session, April 21, 1959, in San Antonio.

A history and physical and pelvic examination with visualization of the cervix is no longer adequate to rule out carcinoma of the cervix. Cytological examination is a practical technique routinely in the detection of cancer. In a 3 year period 1,565 smears were made, with 3 carcinomas of the cervix being found. Additional atypical epithelial changes reflecting lesions needing treatment were recognized.

False negative smears were present in 2 cases. The first was obtained preoperatively in a 31 year old para-76016, who underwent an anterior and posterior repair with amputation of the cervix. The excised portion of the cervix showed a small circumscribed area of carcinoma in situ at the squamocolumnar junction. In this instance the smears were made in a proper manner and, when reviewed in retrospect following the return of the pathological diagnosis, still did not show any tumor cells. The second patient had had punch biopsies of the cervix elsewhere and was referred here because carcinoma of the cervix could not be ruled out on the biopsy material. The smear was negative, but, because of the history, a sharp cone of the cervix was done which showed carcinoma in situ. Both patients were treated by total abdominal hysterectomy, taking a large cuff of the vaginal wall about the cervix.

Carcinoma of the cervix, according to Younge,[4] attacks about 2 per cent of the female population past 30 years of age, killing over 50 per cent of those in whom the diagnosis is made. Approximately 90 per cent of these lesions are in the endocervical canal, and about the same proportion show abnormality of the cervix proper.

In this series 1 carcinoma of the cervix was found on every 521 smears. The annual report of the Meyer Memorial Hospital[5] showed the incidence of recognizable cancer in patients past 30 years of age to be 1 case in every 625 patients examined.

The number of carcinomas in situ of the cervix found was 1.27 per 1,000 smears. According to Stern,[6] 3 per 1,000 smears is to be expected statistically in the general population at large. Ullery and others[7] reporting on 37,540 smears found 2.79 carcinomas in situ of the cervix per 1,000 smears. Younge[4] reported Erickson as finding in 108,000 cases 3.6 carcinomas in situ per 1,000 smears and in the second screening 2.2 per 1,000 smears. We believe that our rate, which is lower than that generally reported, is, in a large part, due to the small number of cases. Our series also includes a group of patients under 30 years of age, and a portion represents repeat smears on the same patients.

The false positives were due in 3 instances to atypical hyperplasia of the cervical epithelium. Pathologists agree that atypical hyperplasia of cervical epithelium is the lesion which is most difficult to distinguish from carcinoma in situ by cytological methods. Soule[8] in 65,571 primary cervical smears reported a false suspicious rate of 2.4 per 1,000 smears. Reagan and others[9] found in following 65 cases of atypical hyperplasia of the cervix from 1½ to 4 years that the lesion regressed in 35 instances and persisted in 20. The diagnosis of carcinoma in

situ of the cervix was made in 9 of these cases, and 1 later proved to have an invasive carcinoma of the cervix. (These statistics would indicate that atypical hyperplasia is not always an innocuous lesion.)

Clinically speaking, the false negative smears present the major problem. The technique, however, tends to give a higher ratio of false positives. Occasionally, false negative smears occur, due to mistaken judgment of the observer reading the smear, faulty collection techniques, and to the fact that on rare occasions malignant tumors do not exfoliate tumor cells. Berg and Bader[2] in assessing the value of cytology in cancer detection found the laboratory error is about 10 per cent in laboratories of moderate experience. When this error is interpreted from the standpoint of the increased mortality from these errors, it is of note that if repeat smears are taken yearly, by the end of 3 years only 1 case in 1,000 would have been missed by cervical cytology alone. At the end of 5 years the error rate of 1 per 100,000 cases is far less than the 1 missed case in the whole country every year. The error decreases with repeat examinations; thus, the only women who need to fear cancer are those whose cancers are so atypical that they will escape detection in 10 or more smears. This is reassuring to all physicians who routinely screen for carcinoma of the cervix using the Papanicolaou technique. It indicates that, with ordinary care, the false negatives, being so few, will not interfere with the value of the procedure.

CONCLUSIONS

Cervical cytology is a definite aid in the detection of early carcinoma of the cervix. All physicians can achieve satisfactory results in early detection of carcinoma of the cervix by including cervical cytology as a part of the annual examination of their female patients.

REFERENCES

A bibliography may be obtained from the authors.

Dr. Kable, Department of Obstetrics and Gynecology, Wichita Falls Clinic-Hospital, Wichita Falls.
Drs. Irvine and Irvine, Bethania Hospital, Wichita Falls.

Clarification of the Doctor-Patient Relationship As a Goal in Brief Psychotherapy

EUGENE A. HARGROVE, M.D.

Raleigh, North Carolina

THE PURPOSE of this paper is to describe a method of teaching psychotherapy to fourth year medical students at the University of North Carolina School of Medicine during their clerkships in the psychiatric and general clinics. The faculty at the university attempted to formulate a treatment method which was brief, goal limited, and oriented but which utilized fundamentals of the psychotherapeutic process, such as, emotional abreaction, insight, and transference. Our aim, however, was not to teach psychotherapy as a special medical technique concerned chiefly with the neuroses and psychoses, but rather to direct attention to the known fundamentals of the doctor-patient relationship which have universal application in the practice of medicine.

As a working definition of psychotherapy we took the simple forthright one of Romano's[6] that, "Psychotherapy is the utilization of psychologic measures in the treatment of sick people." Electing to concentrate on the doctor-patient relationship did focus on transference manifestations, but this also allowed for a certain degree of abreaction in regard to both current and past history and some insight into the origin and nature of the illness as it stemmed from the patient's maladaptive interpersonal reactions.

The therapeutic process was based on the following assumptions: (1) the patient's difficulties in relating to key figures in his present environment stem from limited stereotyped interpersonal patterns; (2) these limited interpersonal patterns produce frustration and lead to the secondary symptoms of anxiety, hysteria, obsessions, and others; and (3) the patient will repeat with the therapist these previously developed stereotyped interpersonal patterns regardless of their appropriateness.

The therapeutic process, arbitrarily limited to a maximum of 25 interviews, consisted of two steps: (1) observation, description, and classification of

the characteristic interpersonal pattern which developed between the patient and the therapist, and (2) clarification of this relationship.

In essence the student physician was to work with a patient with the primary goal of observing, analyzing, and clarifying the interpersonal relation as it developed between him and the patient. Thus, the compulsion to repeat with the physician previously developed interpersonal patterns was to be the basic concept in teaching and understanding the doctor-patient relationship.

To apply this concept clinically it became necessary to pay particular attention to the following three components of the doctor-patient relationship: the behavior of the patient, the attitude of the physician, and the reciprocal relationship which developed.

VERBAL AND NONVERBAL BEHAVIOR

To teach the students to observe and describe the overt, public behavior of a patient became no easy task. They tended to accept verbal communication at face value. The shades and nuances of affective behavior and nonverbal communication were especially elusive and seemed beyond the ken of the majority of our students initially. That the monosyllabic gesture of the hitchhiker, for example, could convey affect such as arrogance, indecision, boredom, pleading, or confidence stretched their credulity.

The student needed to be aware that the verbal and nonverbal components of the patient's behavior do not have to, and frequently do not, denote agreement with each other. Observe the patient who pounds on the desk with his fists while he vociferously declares he is not angry. However, the pounding fist of the angry patient is mechanically identical with the pounding fist of the patient who enthusiastically endorses a point of agreement. In each case it has a different meaning. This meaning is more properly termed affect. It is this affective element of nonverbal language that tends to pull response from another in interpersonal relationships. In other words, one reacts to a gesture according to the affect accompanying its transmission rather than to the sign itself. Kerdman and Peek[3] have pointed out that gestures and facial expressions frequently reveal unconscious responses and reactions while, in contrast, verbal language is used to express conscious defensive operations.

The students gradually began to take cognizance of not only the verbal, but also nonverbal and affective aspects of behavior. Gestures, acts of walking and other movements, display of material things, including clothes, took on a new significance in the evaluation of the patient's total behavior. Thus, another dimension was added to the descriptive behavior.

Dr. Eugene A. Hargrove, director of mental hospitals in North Carolina and associate clinical professor in psychiatry at the University of North Carolina School of Medicine, presented this paper before the Texas Neuropsychiatric Association, April 19, 1959, in San Antonio.

A method of teaching psychotherapy to medical students is aimed at the doctor-patient relationship rather than neuroses and psychoses. The student is taught to work with a patient with the primary goal of observing, analyzing, and clarifying the interpersonal relation as it develops between him and the patient.

The following example was taken from the protocol of a student. The woman could be a patient in almost any doctor's waiting room:

> She is dressed rather elaborately with a low neckline, which she keeps fingering and pulling. She wears a tight skirt which she repeatedly smooths across her knees. She looks interesting sitting there, but she is really more suitably dressed for a date than for a visit to a busy doctor's office. As she waits she swings her leg in a slow, rhythmic, provocative manner watching all the men in the waiting room. She greets the doctor in an overgracious, even coquettish, manner. She walks into his office with swinging hips and almost immediately begins to tell her history in a dramatic, extravagant way, her speech filled with hyperboles. As she talks she continues to finger her clothes in a suggestive manner.

I believe this is more helpful than saying, "The patient is a 28 year old, well proportioned, white female." What is this patient's nonverbal affective behavior communicating to the doctor? On the surface this looks like a sexual invitation.

Or as another example described by a student, observe a man who sits meekly and quietly in the doctor's office:

> He is unusually polite, modest, and self-effacing in his contact with the doctor. He shakes hands limply, blushes easily, smiles hesitantly, rarely looks at the doctor and yes sirs and no sirs him throughout the interview. His movements are halting, indecisive, and sometimes awkward. He looks furtively about the room for an unobtrusive place to sit. His difficulties are mentioned apologetically with downcast or baleful eyes; rising inflections in his sentences make each a tremulous question or appeal. He is attentive to the doctor and sits in childlike adulation at his feet, hanging on every word and making certain he responds with what he thinks the doctor wants to hear. Every statement is offered in a tentative way, and any indication the doctor is impatient causes him to retract or qualify. He parries with self-effacement, submissiveness, and docility. He leans forward in anticipation although his body appears to have little vitality or tone. His head bends forward or draws in. His hands make small confined movements as though staging the patient. His laugh is flat, somewhat hesitant, and easily shut off. He is silent frequently, at-

tempting to encourage the physician to direct the situation while he nods in grateful acknowledgement of the physician's omnipotence.

What is this patient communicating to the doctor? His pattern appears to be one of servitude and respect.

CLASSIFICATION OF RELATIONSHIPS

Once the patient's behavior was described an attempt was made to classify it. Slavson,[7] Courts,[2] and others have proposed classificatory systems for the types of relationship people tend to establish.

Initially in teaching students we used Colby's[1] classification of transference wherein the patient seeks in the doctor one of five relations: a giver of affection, a powerful authority, an ideal model, a rival, or a favorite child. Eventually we came to use a classification of interpersonal behavior formulated by Leary[4] which described the overt, public behavior of the patient, but in addition described feelings most likely to be provoked in others by the patient's behavior. In Leary's scheme interpersonal behavior was classified into 16 mechanisms or reflexes (fig. 1).

Leary has emphasized the surprising ease with which human beings can get others to respond in a uniform and repetitive way. The more severely ill the patient the more limited becomes the interpersonal techniques; he may have abandoned all except one to which others react in a consistent way. Competitive-exploitive behavior may provoke distrust and inferiority. Managerial-autocratic behavior frequently provokes obedience and respect. Docile-dependent behavior leads to advice and help. Skeptical-distrustful behavior provokes punishment and rejection. Modest self-effacing behavior evokes arrogance and leadership, whereas blunt-aggressive behavior provokes hostility and resistance.

We utilized this classification of interpersonal behavior for two reasons: it was useful in classifying transference reactions and it introduced the doctor's response to the patient. Strictly speaking, Leary's classification was not of transference phenomena; it dealt with adaptive as well as pathologic behavior patterns. However, the rigid interpersonal reflex categories were similar to attitudes which patients transferred to their doctors. Another interesting aspect of this classification scheme, although not explicitly stated as a part of it, was the similarity of the several interpersonal categories to the phases of relationship through which humans pass during their growth and development. These are dependent, aggressive, competitive, and responsible, or in terms of psychoanalytic nomenclature, oral, anal, phallic, and genital. To be specific in regard to Leary's diagram, if we start at one point on the outer circle we find dependent relationships which lead next to aggressive then to competitive and finally to cooperative responsible interpersonal behavior.

Although Leary's classification appropriately emphasized the doctor's response to the patient, we did not consider these necessarily as counter-transference manifestations, but rather the natural expected response drawn from the doctor by the patient's specific behavior. For example: dependent behavior evokes help and advice. It is well and good to expect the student physician to be relatively free of serious emotional problems, to teach him that his attitude should generate confidence and understanding and that his response must be sensitive, flexible, emphatic, but objective. However, the doctor has his own feelings and reacts to different patients in various ways: to one with irritation, to another with interest, to a third with distrust, and so on. His reactions may give a valuable clue as to what type of relationship the patient is developing. It becomes necessary for a doctor to observe his own reactions to the patient's conduct not only to understand the patient, but also to minimize counter-responses and behavior which interfere with treatment by creating distrust, competition, docility, or undue dependence in the patient.

We think that many untoward reactions, such as inflexibility, over-identification, undue authoritarianism, withdrawal, arrogance, and rejection, which the student doctor shows in relationship with the patient come about not necessarily from personality deficits of the student physician, but from his lack of understanding of the reciprocal nature of the doctor-patient relationship.

In order to illustrate this reciprocal relationship let us return to the modest self-effacing patient we discussed earlier and try to understand what he is communicating to the doctor and the doctor's response. This weak, timid, limp handshake says, "Treat me gently; lead me by the hand just as you would a lost child." His attire says, "I have dressed so as not to attract attention." The hesitant apologetic manner in which he talks about his particular problem tells the doctor to note how much difficulty he has in doing things for himself; he must regretfully ask for help and advice. These actions all tend to evoke in the physician a desire to help, advise, or lead the patient out of his difficulties. The entire overt behavior telegraphs the message, "I am weak, you are strong, help me." A problem arises when the doctor's response interferes with treatment by reinforcing the docility or undue dependence.

To aid us in teaching the components of the doctor-patient relationship, particularly the interaction, we counted heavily on clinical material with considerable supervision. Frequently one instructor interviewed the patient behind the one way screen

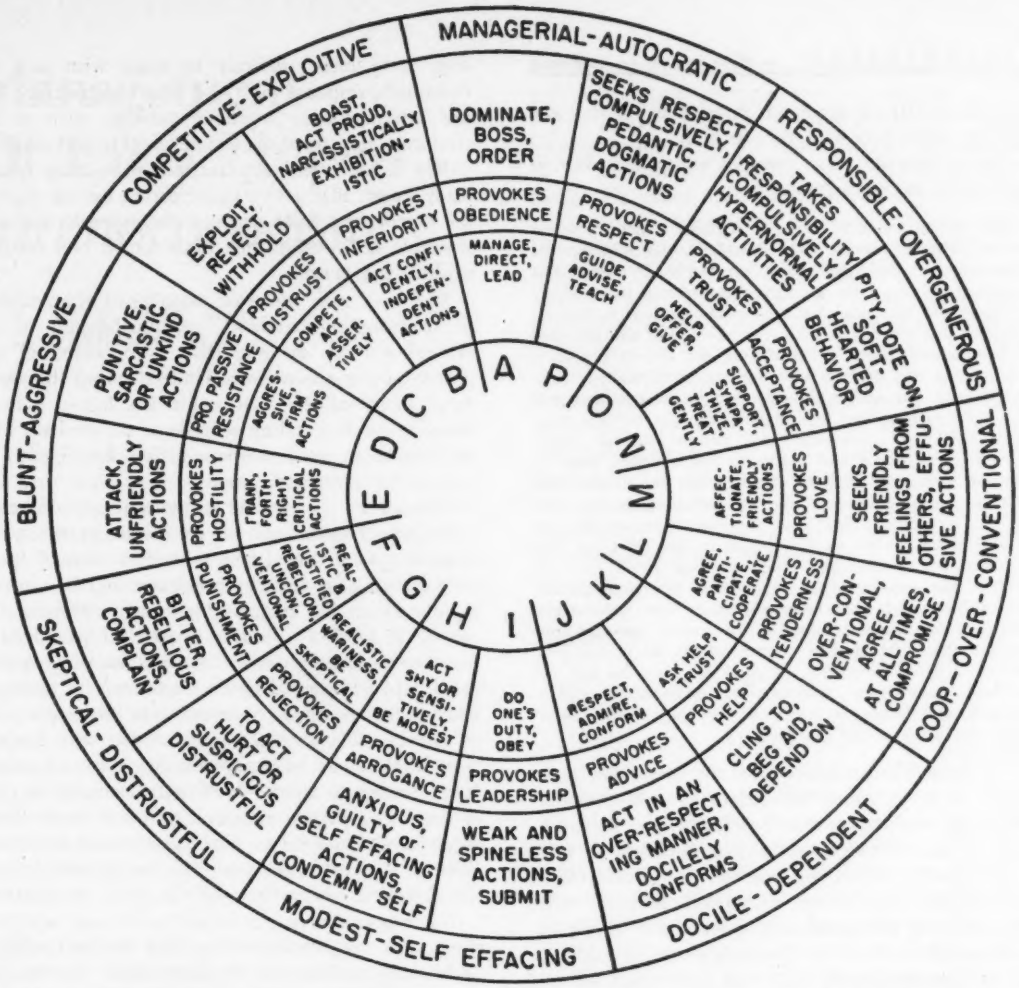

Fig. 1. Classification of interpersonal behavior into 16 mechanisms or reflexes. Each of the 16 interpersonal variables is illustrated by sample behaviors. The inner circle names adaptive reflexes, such as manage. Proceeding outward, the next ring indicates the type of behavior that this interpersonal reflex tends to "pull" from the other one; thus the person who uses the reflex A tends to call up in others obedience. These findings involve two-way interpersonal phenomena—what the subject does and what the other does in return—and are therefore less reliable than the other interpersonal categories presented in the inner and outer rings. The next circle illustrates extreme or rigid reflexes, such as dominates. The perimeter of the circle is divided into eight general categories employed in interpersonal diagnosis. Each of these general categories has a moderate (adaptive) and an extreme (pathological) intensity, such as managerial-autocratic. (After Leary, T.: Theory and Measurement Methodology of Interpersonal Communication, Psychiatry 18:147-161 [May] 1955.)

while another instructor conducted a running commentary of the process. In addition we used a series of short films based on actual clinical interviews, although the filming itself was staged. These films illustrating several reactions which patients manifest, such as dependency, aggression, hostility, and competition, were not used as cinematographic theses but as illustrative points in discussion groups. Each film sequence had two parts—the first part illustrated how an inexperienced therapist conducted the interview and the second, hopefully, how a more experienced therapist would react to the same patient. The value of these films was in focusing on the reciprocal relationship and the lively discussions provoked.

CLARIFYING RELATIONSHIP

At this point in our teaching we hoped the student had become familiar with the components of the doctor-patient relationship, that is, the patient's personality pattern, the doctor's attitude, and the interaction. We turned our attention at long last to the treatment process, which hinges on the simple prin-

ciple of clarifying the kind of relationship that the patient establishes with the doctor.

As an example let us consider a case described in one of the student's protocols.

The patient was a 21 year old engaged woman, a senior at the university, whose chief complaint was anxiety. Her symptoms had developed when her fiance, in anger, had suggested delaying the marriage because she was making so many pre and post marriage plans without consulting him. She was a pretty woman, extremely alert and attentive in her manner, immediately making the student physician feel that he was dealing with a sharp, sophisticated, business woman. She wore a shoulder bag which was large and which she manipulated in a manner reminiscent of a portfolio. She was conversant with current notions about psychiatric treatment and began to describe her story in terms of seemingly lifelong conflict with her mother and sister and great admiration for her father, a wealthy, successful businessman. Many of the characteristics she described in her father were reflected in her behavior. She described her mother and sister as weak-willed and dependent. She soon provided behavior in the doctor-patient relationship which was characteristic of her relationship with men. At the beginning of the fourth interview the patient entered the student doctor's office, sat in the doctor's chair behind the desk, plopped her shoulder bag on the desk, broke out a cigarette, lit it, settled back with a few puffs and began the interview with the remark, "Now where did we leave off last time?"

The patient had repeated with the doctor the managerial behavior which had led to her interpersonal difficulties and anxiety with her fiance. Her behavior with the doctor was uncritically pointed out to her, to which information she reacted with considerable surprise. Her dominating, managerial behavior was repeatedly but sympathetically pointed out to her as it continued to occur in relationship with the doctor and its appropriateness with him questioned. In 15 interviews, her interpersonal relations improved and her anxiety was reduced significantly.

Time and again, however, during therapy the students responded with what we deemed less than constructive attitudes. Responses occurred which reinforced competition, distrust, docility, or undue dependence. Take, for example, a docile dependent young man for whom the student therapist volunteered to hand carry a note of excuse across campus.

EVALUATION

I wish I could report that this treatment method has proved smashingly successful. There have been some spectacular results noted clinically and on projective tests. We often were pleased with the constructive modifications of crippled interpersonal reactions following treatment. However, as might be expected, the patients who were more severely regressed in their interpersonal relations, that is, the dependent, the distrustful, the skeptical, the aggressive, were more difficult to work with and the therapist's response to these less constructive. The less interpersonally regressed patients, such as the rivalrous ones, responded more quickly and easily.

We have increasingly realized something we already knew, that active participation on the part of the doctor in a brief dynamic therapy calls for considerable skill—more than most fourth year medical students can muster.

We have not, however, abandoned this method in teaching the students, mainly because it has offered a focus on important components in the doctor-patient relationship. Understanding the reciprocal nature of the relationship has led to a more objective, understanding attitude in the student. This we believe in itself, without active intervention, is a powerful therapeutic tool.

We are all aware that as the student progresses and matures in his education changes occur in his attitude toward the patient as well as himself. Some of these changes have been documented in a sociologic study of the student physician by Merton and others.[5] A kind of objective interest without detachment and a willingness to help in spite of problems is perhaps an optimal type of relationship. Students who are best equipped to meet the technical demands of the physician's role are also those who find it least difficult to meet its attitudinal requirements. If the student is able to work with technical facility in the doctor-patient relationship, he is much more objective and helpful in his attitude toward patients whether they be anxious, angry, overconcerned, hostile, querulous, demanding, or just plain cooperative.

We believe this particular method of teaching psychotherapy has provided us a catalyst for the normally developing constructive attitudes which the student comes to hold toward himself and the patient.

However, any evaluation of teaching methods must take into consideration intellectual accomplishments, attitudinal factors, and motivational forces. This complex task in regard to our method we have only begun.

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♦ Dr. Hargrove, P. O. Box 70, Raleigh, N. C.

Management Of Early Hyperadrenocorticism

R. V. FORD, M.D. and
R. C. OVERTON, M.D.

Houston, Texas

THE AVERAGE practitioner sees many patients with early hyperadrenocorticism. They present themselves to the practitioner with the condition masquerading under various and bizarre complaints. They may be obese, hypertensive, mildly diabetic, hirsute, oligomenorrheic, edematous without any other explanation, complaining of low back pain, or emotionally unstable.

Many of these patients will be labeled as neurotic. It is our purpose to emphasize the necessity to diagnose abnormal adrenal cortical function at an early stage and to recommend early therapy for these patients. The diagnosis is established by the determination of the adrenal steroid excretion in these patients before and after stimulation by adrenocorticotrophic hormone. If they are found to be abnormal and the studies are repeatedly abnormal, the clinician must consider the relief of this syndrome by total adrenalectomy.

We postulate that hyperadrenocorticism is a cyclical disease which rarely is self-limited. Most commonly it is progressive. The degree of willingness to subject the patient to this rather drastic procedure of adrenalectomy is proportional to the knowledge of the clinician regarding the prognosis of untreated hyperadrenocorticism. It is a fairly general opinion that this disease is not totally benign.[7] To illustrate this approach to the management of early hyperadrenocorticism, data are presented concerning 16 such patients who have been observed over the past 2 years.

MATERIALS AND METHODS

Vital statistics of the first 16 patients are presented in table 1. There were 1 male and 15 female patients. The general symptomatology of hyperadrenocorticism constituted the primary surgical indication in 9 of these patients; severe intractible hypertension was the primary indication in 6 patients and incapacitating masculinization with mild hyperadrenocorticism in 1 patient. These patients had received therapy including diet, psychotherapy, and diuretic agents as well as the usual antihypertensive measures.

The crucial diagnosis in these patients was made by observation of the 24 hour excretion in the urine of 17 ketosteroids and 17 ketogenic steroids (primarily glucocorticoids). They were analyzed by the Norymberski technique.[4, 5] Twenty-four hour urine collections were obtained prior to and following two injections (at 12 hour intervals) of corticotrophin zinc, 80 units, intramuscularly. These studies were repeated at 30 to 60 day intervals until it was determined that the patient was in an advancing or persistent state of hyperadrenocorticism. The criteria for total adrenalectomy in this initial group of patients have been (1) an increase in the excretion of 17-ketogenic steroid to at least a three-fold extent following ACTH stimulation contemporaneous with an absolute increase of 50 mg. per 24 hours, and (2) a persistent or advancing clinical syndrome in spite of adequate medical management.

RESULTS

The transabdominal approach was selected for the removal of both adrenal glands permitting an adequate abdominal exploration for coexisting diseases. Hydrocortisone was not used as a preoperative prime contrary to previous recommendations in the literature.[1, 2, 3, 8, 9] At the beginning of the procedure, through a separate intravenous injection, 100 mg. of hydrocortisone in 1,000 cc. of 5 per cent glucose in normal saline solution was started at a slow rate. Thus, in the usual case, after both adrenals have been removed, the patient has received approximately 20 to 40 mg. of hydrocortisone. Blood replacement varied from none in those cases in which blood loss was minimal to a maximum of 4 units. Although the blood replacement in the usual case was relatively small, it is exceedingly important that one attempt to be accurate with this replacement since a deficit at this point greatly complicates further postoperative management.

Dr. R. V. Ford and his co-author offer this paper from the Departments of Medicine, Pharmacology, and Surgery, Baylor University College of Medicine, and the Methodist Hospital.

Diagnosis of hyperadrenocorticism at an early stage when it is largely functional is important. This condition commonly is progressive and not entirely benign. Treatment by total adrenalectomy is simple and has proved of distinct benefit to 16 patients followed for periods of 6 to 30 months.

Accurate and repeated observations of the vital signs together with the hourly urinary output provide the indices for the subsequent amounts of supportive medications needed (table 2). Maintenance of normotensive blood pressure levels and an adequate urine output are the principal goals. Vasopressor agents are not necessary and probably are contraindicated as these patients can and will maintain an adequate blood pressure if hydrocortisone and moderate amounts of salt are administered.

The requirement for hydrocortisone postoperatively is somewhat less in this group of patients than the surgical literature would indicate.[1, 2, 3, 8, 9] During the first 24 hours including surgery the average hydrocortisone requirement has been 200 mg. intravenously (constant slow infusion). Occasionally, more than 9 Gm. of sodium chloride is necessary, particularly, if the patient has been on a severe diuretic regimen preoperatively. The volatile temperature response of these patients often affords an index as to the necessity for a more rapid administration of hydrocortisone. The presence of a persistent tachycardia in the immediate postoperative period is a good indication that the patient is either hypovolemic or deficient in hydrocortisone replacement. Repeated determination of the hematocrit level and of serum and urine electrolytes has not been of practical help in the management of these cases. The usual postoperative salt and hydrocortisone therapy is presented in table 3.

TABLE 1.—*Preoperative Findings in 16 Patients with Functional Adrenal Hypercorticism.*

Age (yr.)		Sex		Significant Hyperadrenocorticism	Symptomatology	
Average	Range	Male	Female		Hypertension	Masculinizing
35	18-53	1	15	9	6	1

TABLE 2.—*Indices to Immediate Postoperative Problems Following Total Bilateral Adrenalectomy.*

Indices	Primary Hydrocortisone Deficiency	Primary NaCl Deficiency	Hypovolemia
Blood pressure	marked decrease	decrease	decrease
Pulse rate	increase	no change	marked increase
Urine flow	decrease	decrease	decrease
Temperature	increase	no change	no change

TABLE 3.—*Postoperative Management of Total Adrenalectomy.*

Day	Hydrocortisone mg.	Route	NaCl Gm.	Route	Water Liters	Route
Operative	200	I.V.	9	I.V.	3	I.V.
1	150	I.V.	9	I.V.	3	I.V.
2	100	I.V.	9	I.V.	2	I.V.
	100	P.O.			1	P.O.
			Regular Diet			
3	120	P.O.	0	P.O.	2	P.O.
4	60	P.O.	9	P.O.	3	P.O.
5-10	40	P.O.	9	P.O.	3	P.O.

The mortality in this series of 16 cases has been 0 and the morbidity has been minimum. This has been true despite the fact that many of these patients presented severe hypertensive cardiovascular problems preoperatively. It is thought that the simple management of these problems has been possible since the diagnosis has been made early and definitive therapy has been carried out before irreversible physiological changes occur.

Preoperative and postoperative photographs (fig. 1-4) nicely demonstrate typical examples characterizing the two broad groups of the series, namely, general hypercorticism and hypertension with associated adrenal hyper-responsiveness. Of the general symptoms relieved by adrenalectomy, weakness, emotional instability, menstrual irregularities, edema,

Fig. 1a. Preoperative photograph of a 28 year old woman with early hyperadrenocorticism.
b. Photograph of the same woman, 3 months following total adrenalectomy.

Fig. 2a. Preoperative photograph of a 43 year old woman with mild hyperadrenocorticism and premalignant hypertension.
b. Six weeks postoperatively.

and hirsutism would be significant—more than 90 per cent improvement.

The important objective data presenting clinical improvement are summarized in table 4. The preoperative excretion of 17-ketogenic steroid was elevated and demonstrated an abnormal increase following ACTH injection. The absence of adrenal tissue following surgery is proven by the failure to respond to ACTH. The preoperative blood pressure averaged 170/110 mm. of mercury while the postoperative blood pressure was 120/80. The reduction of blood pressure as well as alterations in the metabolism of salt and water following adrenalectomy has been extremely beneficial to the group of patients presenting problems involving the cardiovascular system. The body weight in the preoperative state averaged 204 and in the postoperative state at the end of 3 months averaged 171 pounds. This is not to imply that total adrenalectomy is feasible therapy for obesity but merely to indicate that obesity is one of the problems of hyperadrenocorticism which can be controlled by the procedure in most instances.

Fig. 3a. Preoperative photograph of a 37 year old woman with severe hypertension and Cushing's syndrome.
b. Six weeks postoperatively.

Fig. 4a. Preoperative photograph of a 32 year old woman with mild hypertension, oligomenorrhea, weakness, back pain, and hypoglycemia.
b. Body configuration demonstrating central obesity, striae, plethora, and hirsutism.
c. Six weeks postoperatively.

The patient who was operated on primarily for masculinizing tendencies with abnormal menstrual periods and gross enlargement of the clitoris has experienced a return of the menstrual cycle to normal and a 50 per cent reduction in the size of the clitoris in less than 3 months. It may be of additional interest that the patient with the greatest degree of 17-ketogenic steroid (and not 17-ketosteroid) excretion following ACTH presented the operative findings of Stein-Leventhal ovary. Nevertheless, this patient was also subjected to a total adrenalectomy. She has demonstrated a return to normal in body weight and body contour, marked decrease in hirsutism, and establishment of normal menstrual periods. The average hospital stay for the group was 9 days. At the end of 3 months the average dose of oral hydrocortisone required for maintenance was 7 mg. per day.

TABLE 4.—*Preoperative Values of 17-Ketogenic Steroids and the Changes in Blood Pressure and Body Weight 3 Months Following Total Adrenalectomy.*

	17-Ketogenic Steroids (mg./24 hr.) Preoperatively		Body Weight (lb.)		Blood Pressure (cm. Hg.)	
Patient	Before ACTH	After ACTH	Preop.	Postop.	Preop.	Postop.
1	16	84	157	133	15/11	10/6
2	19	124	167	136	12/9	11/8
3	22	129	158	121	15/10	11/7
4	30	192	178	135	19/11	12/8
5	42	140	226	200	15/10	12/8
6	44	202	300	269	18/12	15/10
7	32	100	301	253	20/12	15/10
8	59	123	190	150	18/12	12/8
9	39	113	110	104	11/8	11/8
10	30	140	241	190	17/11	13/8
11	34	228	180	174	20/12	15/10
12	115	309	180	130	16/10	11/8
13	39	151	203	178	16/11	12/8
14	26	221	220	167	25/14	11/6
15	36	106	220	181	15/7	11/8
16	11	184	230	210	20/13	12/8
Av.	37	159	204	171	17/11	12/8

DISCUSSION

The purpose of this paper is to present a plea for the early diagnosis of hyperadrenocorticism, Cushing's syndrome. This demands an alertness on the part of the practitioner to study patients presenting the following predominant problems: (1) obesity, (2) functional hypoglycemia, (3) diabetes, (4) hypertension, (5) emotional instability or overt psychiatric disturbances, (6) osteoporosis, (7) oligomenorrhea, (8) masculinization with hirsutism and so forth, and (9) edema without obvious explanation.

Many of these patients should receive the benefit of an assessment of adrenal cortical function. This has been fairly well simplified by the availability of laboratory techniques for the estimation of adrenal steroids. We have elected to analyze the 17-ketosteroids and 17-ketogenic steroids by the Norymberski technique.[5] We also have explored the levels of plasma hydrocortisone in these patients. Many patients with early hyperadrenocorticism demonstrate normal excretion of these steroids in the control 24 hour urine, but after stimulation with adrenocorticotrophic hormone (corticotrophin zinc, 80 units twice over a 12 hour period followed by a second 24 hour urine test) many patients will demonstrate an exaggerated response. We have elected the criteria of at least a three-fold increase in the ketogenic steroid excretion compared to control or at least an absolute increase of 50 mg. per 24 hours. The plasma hydrocortisone level may be an additional corroborative laboratory technique, and our normal values for this are 25 gamma per 100 cc. of blood in the control state and 45 gamma per 100 cc. of blood after stimulation with ACTH. It is to be emphasized that these studies should be repeated at 30 to 60 day intervals.

When the responsiveness is seen to be consistent or more marked and when the patient continues to present the clinical syndrome, consideration should be given for surgical relief of this condition. At the present time we believe that the radical procedure of total adrenalectomy is the procedure of choice. This is a new concept which has been made practical by the availability of satisfactory replacement therapy in the form of hydrocortisone. It is to be emphasized that the dose of orally administered hydrocortisone is quite low for these patients.

The long term management of these patients may present a challenge to the clinician and may be one of the factors which would detract him from recommending definitive therapy for the condition. The patients must be made aware of the necessity to take oral hydrocortisone for the rest of their lives (usually), and they must be educated as to the increased requirements of hydrocortisone during periods of stress, such as infections and emotional upsets.

However, the results of this study indicate that the procedure for the removal of the adrenal glands is simple, the postoperative convalescence is rapid, and the subjective and objective benefits following this procedure are gratifying.

It is impossible to discuss this problem without expressing a definite need for a chemotherapeutic agent which will accomplish the same result as total adrenalectomy for these patients. This need is felt even more in those patients who present borderline states of hyperadrenocorticism. Pharmacologic research is making progress slowly in this direction.

CONCLUSIONS

Sixteen patients have been observed and treated for functional hyperadrenocorticism by total adrenalectomy. They have been followed for periods of 6 to 30 months and have received distinct benefit from this procedure. These patients have been treated at a stage of their disease which may be considered to be of a functional nature. Emphasis on the ease and simplicity of this form of management is presented. We also wish to emphasize the importance of early diagnosis.

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Dr. Ford, 5206 Richmond Avenue, Houston 27.
Dr. Overton, Hermann Professional Building, Houston.

★ Coming Meetings

Texas Medical Association, Fort Worth, April 9-12, 1960 (Executive Board, Jan. 17, 1960). Dr. F. W. Yeager, Corpus Christi, Pres.; Mr. C. Lincoln Williston, 1801 North Lamar Blvd., Austin, Exec. Secy.

American Medical Association, Dallas (Clinical Session), Dec. 1-4, 1959. Dr. Louis M. Orr, Orlando, Fla., Pres.; Dr. F. J. L. Blasingame, 535 North Dearborn, Chicago 10, Exec. Vice-Pres.

Current Meetings

DECEMBER

American Academy of Dermatology and Syphilology, Chicago, Dec. 5-10, 1959. Dr. A. C. Cipollaro, New York, Pres.; Dr. Robert R. Kierland, Mayo Clinic, Rochester, Minn., Secy.

Southern Surgical Association, Hot Springs, Va., Dec. 8-10, 1959. Dr. George C. Finney, Baltimore, Pres.; Dr. John D. Martin, Jr., Emory University, Ga., Secy.

Texas Academy of Internal Medicine, San Antonio, Dec. 4-5, 1959. Dr. Merton M. Minter, San Antonio, Pres.; Dr. Hugo T. Engelhardt, 1216 Main, Houston, Secy. Meetings restricted to members.

Texas Division, American Cancer Society, Austin, Dec. 10-12, 1959. Dr. John A. Wall, Houston, Pres.; Mr. Curt W. Reimann, 5014 Bull Creek Rd., Austin 3, Executive Director.

Texas Rheumatism Association, San Antonio, Dec. 4, 1959. Dr. Warren W. Moorman, Fort Worth, Pres.; Dr. J. Morris Horn, 3707 Gaston, Dallas, Secy.

Texas Society of Ophthalmology and Otolaryngology, Fort Worth, Dec. 4-5, 1959. Dr. James T. Robison, Austin, Pres.; Dr. Edwin G. Grafton, 4319 Oak Lawn, Dallas, Secy.

Texas State Board of Medical Examiners, Fort Worth, Dec. 3-5, 1959. Dr. M. H. Crabb, Fort Worth, Secy.; Mrs. Luanna Reddin, 1714 Medical Arts Bldg., Fort Worth, Assistant Secy.

JANUARY

American Academy of Allergy, Hollywood-by-the-Sea, Fla., Jan. 11-13, 1960. Dr. Francis C. Lowell, Boston, Pres.; Dr. Joseph Noah, 100 N. Euclid Ave., St. Louis 8, Mo., Secy.

Texas Radiological Society, Houston, Jan. 22-23, 1960. Dr. Herman C. Sehested, Fort Worth, Pres.; Dr. R. P. O'Bannon, 1216 Pennsylvania, Fort Worth, Secy.

Texas Urological Society, Waco, January 23-24, 1960. Dr. William Heck, San Antonio, Pres.; Dr. Moreton A. Magid, 1525 Colcord Ave., Waco, Secy.

Twelfth District Society, Marlin, January 12, 1960. Dr. Paul H. Mitchell, Corsicana, Pres.; Dr. J. M. Brown, Torbett Clinic, Marlin, Secy.

International Medical Assembly of Southwest Texas, San Antonio, Jan. 25-27, 1960. Dr. Alvin O. Severance, San Antonio, Pres.; S. E. Cockrell, 202 W. French Place, San Antonio, Exec. Secy.

National and Regional

American Academy of General Practice, Philadelphia, March 19-24, 1960. Dr. Fount Richardson, Fayetteville, Ark., Pres.; Mr. Mac F. Cahal, Volker Blvd. at Brookside, Kansas City 12, Executive Secy.

American Academy of Ophthalmology and Otolaryngology. Dr. John H. Dunnington, New York, Pres.; Dr. W. L. Benedict, 15 Second St. S.W., Rochester, Minn., Secy.

American Academy of Pediatrics, Atlantic City, April 20-22, 1960. Dr. William W. Belford, San Diego, Calif., Pres.; Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Director.

American Association for Maternal and Infant Health. Dr. M. Edward Davis, Chicago, Pres.; Mrs. Patricia Dorr, 116 S. Michigan Ave., Chicago 3, Executive Director.

American Association for Thoracic Surgery, Miami Beach, May 11-13, 1960. Dr. William E. Adams, Chicago, Pres.; Dr. Hiram T. Langston, 7730 Corondelet Ave., St. Louis 5, Secy.

American Association of Genito-Urinary Surgeons, Dearborn, Mich., May 11-13, 1960. Dr. Reed M. Nesbitt, Ann Arbor, Mich., Pres.; Dr. W. J. Engel, 2020 E. 93rd St., Cleveland 6, Secy.

American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8-10, 1960. Dr. Robert A. Ross, Chapel Hill, N. C., Pres.; Dr. Clyde L. Randall, 216 Summer St., Buffalo 22, Secy.

American Association of Plastic Surgeons, Milwaukee, May 17-20, 1960. Dr. Lyndon A. Peer, New Jersey, Pres.; Dr. Thomas D. Cronin, 6615 Travis St., Houston 25, Secy.

American Cancer Society, New York, Oct. 26-27, 1960. Dr. Warren H. Cole, Chicago, Pres.; Mr. Granville Whittlesey, 521 West 57th St., New York 19, Secy.

American College of Allergists, Miami Beach, Feb. 28-March 4, 1960. Dr. Cecil M. Kohn, Kansas City, Pres.; Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis, Executive Vice-Pres.

American College of Chest Physicians, Miami Beach, Fla., June 8-12, 1960. Dr. Seymour M. Farber, San Francisco, Pres.; Mr. Murray Kornfeld, 112 E. Chestnut, Chicago 11, Executive Director.

American College of Gastroenterology, Philadelphia, Oct. 23-29, 1960. Dr. Joseph Shaiken, Milwaukee, Pres.; Mr. Daniel Weiss, 33 West 60th, New York 23, Executive Director.

American College of Obstetricians and Gynecologists, Cincinnati, April 3-6, 1960. Dr. John I. Brewer, Chicago, Pres.; Mr. Donald F. Richardson, P. O. Box 749, Chicago 90, Executive Secy.

American College of Physicians, San Francisco, April 4-8, 1960. Dr. Howard P. Lewis, Portland, Ore., Pres.; Mr. E. R. Loveland, 4200 Pine, Philadelphia 4, Secy.

American College of Radiology, New Orleans, Feb. 3-6, 1960. Dr. Lawrence Reynolds, 10 Peterboro, Detroit, Pres.; Mr. W. C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons. Dr. Newell W. Philpott, Montreal, Pres.; Dr. Michael L. Mason, 40 E. Erie, Chicago 11, Secy.

American Congress of Physical Medicine and Rehabilitation, Washington, D.C., Aug. 21-26, 1960. Dr. F. J. Kottke, Minneapolis, Pres.; Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secy.

American Dermatological Association, Boca Raton, April 8-12, 1960. Dr. Marion B. Sulzberger, New York, Pres.; Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Secy.

American Gastroenterological Association, New Orleans, March 31-April 2, 1960. Dr. H. Marvin Pollard, Ann Arbor, Pres.; Dr. Wade Volwiler, Secy., University of Washington School of Medicine, Seattle 5.

American Gynecological Society, Williamsburg, Va., May 30-June 1, 1960. Dr. Karl H. Martzloff, Portland, Pres.; Dr. A. A. Marchetti, 3800 Reservoir Rd. N.W., Washington 7, D. C., Secy.

American Heart Association, St. Louis, Oct. 21-25, 1961. Dr. A. Carlton Ernstene, Cleveland, Pres.; Mr. William F. McGlone, 44 E. 23rd, New York 10, Secy.

American Hospital Association, San Francisco, Aug. 29-Sept. 1, 1960. Dr. Russell A. Nelson, Baltimore, Md., Pres.; Dr. Edwin L. Crosby, 18 E. Division Street, Chicago, Executive Director.

American Laryngological, Rhinological, and Otological Society, Miami Beach, March 15-17, 1960. Dr. Theodore E. Walsh, St. Louis, Pres.; Dr. C. S. Nash, 708 Medical Arts Bldg., Rochester, N. Y., Secy.

American Neurological Association, Boston, June 13-15, 1959. Dr. Derek Denny-Brown, Boston, Pres.; Dr. Melvin D. Yahr, New York Neurological Institute, 710 W. 168th Street, New York 32, Secy.

American Ophthalmological Society, Colorado Springs, May 16-18, 1960. Dr. A. B. Reese, New York, Pres.; Dr. M. C. Wheeler, 30 W. 59th, New York 19, Secy.

American Orthopaedic Association, Hot Springs, Va., May 30-June 2, 1960. Dr. John Royal Moore, Philadelphia, Pres.; Dr. Lee Ramsay Straub, 535 East 70th St., New York 21, Secy.

American Pediatric Society, Swampscott, Mass., May 5-6, 1960. Dr. Samuel Z. Levine, New York, Pres.; Dr. A. C. McGuinness, Room 1036, 2800 Quebec St., N.W., Washington 8, D. C., Secy.

American Proctologic Society, Houston, April 25-27, 1960. Dr. H. R. Reichman, Salt Lake City, Pres.; Dr. Norman D. Nigro, 10 Peterboro, Detroit 1, Secy.

American Psychiatric Association, Atlantic City, N. J., May 9-13, 1960. Dr. William Malamud, New York, Pres.; Dr. C. H. Hardin Branch, 156 Westminister Ave., Salt Lake City, Secy.

American Public Health Association, San Francisco, Oct. 31-Nov. 4, 1960. Dr. Malcolm H. Merrill, Berkeley, Calif., Pres.; Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, Executive Secy.

American Society of Anesthesiologists, New York, Oct. 2-7, 1960. Dr. J. Earl Remlinger, Jr., Wilmette, Ill., Pres.; Dr. Robert L. Patterson, 612 Bershire Drive, Pittsburgh 15, Secy.

American Society of Clinical Pathologists, Chicago, Sept. 24-Oct. 2, 1960. Dr. John J. Clemmer, Albany, Pres.; Mr. Claude E. Wells, 445 Lake Shore Drive, Chicago 11, Executive Secy.

American Surgical Association, White Sulphur Springs, W. Va., April 3-6, 1960. Dr. Warren H. Cole, Chicago, Pres.; Dr. William Altemeier, Cincinnati General Hospital, Cincinnati 29, Secy.

American Urological Association, Chicago, May 16-19, 1960. Dr. William M. Coppridge, Durham, N. C., Pres.; Mr. William P. Didusch, 1120 N. Charles St., Baltimore 1, Executive Secy.

Association of American Physicians and Surgeons, St. Louis, Sept. 29-Oct. 1, 1960. Dr. Louis Wegryn, Elizabeth, N. J., Pres.; Mr. Harry E. Northam, 185 N. Wabash Ave., Chicago 1, Executive Director.

International College of Surgeons, U. S. Chapter, Rome, Italy, May 15-18, 1960. Dr. Henry Meyerding, Rochester, Minn., Pres.; Dr. Ross T. McIntire, 1516 Lake Shore Dr., Chicago, Executive Director.

National Tuberculosis Association, Los Angeles, May 15-20, 1960. Dr. H. McLeod Riggins, New York, Pres.; Mrs. Wallace B. White, 651 Marlborough Rd., Brooklyn, Secy.

Radiological Society of North America. Dr. Lawrence L. Robbins, Boston, Pres.; Dr. Donald S. Childs, 713 E. Genesee, Syracuse 2, N. Y., Secy.

South Central Association of Blood Banks, Albuquerque, March or April, 1960. Dr. John B. Alsever, Phoenix, Pres.; L. Ruth Guy, Ph.D., Room 1101, Stonleigh Hotel, Dallas, Secy.

Southern Medical Association. Dr. Edwin Hugh Lawson, New Orleans, Pres.; Mr. V. O. Foster, 2601 Highland Ave., Birmingham 5, Executive Secy.

Southern Psychiatric Association, Virginia Beach, Va., Oct. 2-4, 1960. Dr. David A. Wilson, Charlottesville, Va., Pres.; Dr. Richard Proctor, Winston-Salem, N. C., Secy.

Southwest Allergy Forum, Oklahoma City, April 2-5, 1960. Dr. Johnny A. Blue, Oklahoma City, Pres.; Dr. George L. Winn, Suite 104, Lister Medical Building, 430 Northwest Twelfth St., Oklahoma City, Secy.

Southwest Regional Cancer Conference. Dr. W. S. Lorimer, Jr., Fort Worth, Chm.; Mrs. Ira Frances Ball, 264 W. 11th, Fort Worth, Secy.

Southwestern Medical Association, El Paso, Oct. 20-22, 1960. Dr. Russell Deter, El Paso, Pres.; Dr. M. D. Thomas, 1501 Arizona St., 12-D, El Paso, Secy.

Southwestern Society of Nuclear Medicine, New Orleans, March 14-15, 1960. Dr. Herbert C. Allen, Jr., Houston, Pres.; Dr. J. R. Maxfield, Jr., 2711 Oak Lawn Avenue, Dallas, Secy.

Southwestern Surgical Congress, Las Vegas, Nev., March 28-31, 1960. Fort Smith, Ark., Dr. Fred H. Krock, Fort Smith, Ark., Pres.; Mary O'Leary, 813 Medical Arts Bldg., Oklahoma City, Exec. Secy.

Tri-State Medical Assembly. Dr. R. B. Langford, Shreveport, Pres.; Dr. J. W. Wilson, Jr., 940 Margaret Place, Shreveport, Secy.

United States-Mexico Border Public Health Association, Hermosillo, Sonora, Mex., April 4-8, 1960. Mr. Frank J. Von Zuben, Jr., Austin, Pres.; Dr. Jorge Román, 243 United States Court House, El Paso, Secy.

State

Private Clinics and Hospitals Association of Texas. Dr. Jack S. Maxfield, Dallas, Pres.; Mr. J. J. George, 3404 54th St., Lubbock, Executive Secy.

Texas Academy of General Practice, Dallas, Oct. 3-5, 1960. Dr. E. Sinks McLarty, Galveston, Pres.; Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Executive Secy.

Texas Air-Medics Association, Fort Worth, April 9-11, 1960. Dr. W. W. Sumner, Fort Worth, Pres.; Dr. C. F. Miller, P. O. Box 1338, Waco, Secy.

Texas Association for Mental Health, Austin, Feb. 18-20, 1960. Paul Southern, Ph.D., Abilene, Pres.; Mr. John Lane, 2410 San Antonio, Austin, Executive Director.

Texas Association of Obstetricians and Gynecologists, Austin, February 12-13, 1960. Dr. Maurice Meynier, Houston, Pres.; Dr. Hugh W. Savage, 815 Fifth Ave., Fort Worth, Secy.

Texas Association of Public Health Physicians, Fort Worth, April 10, 1960. Dr. Fred K. Laurentz, Houston, Pres.; Dr. B. M. Primer, 2708 Rio Grande, Austin, Secy.

Texas Chapter, American College of Chest Physicians, Fort Worth, April 10, 1960. Dr. L. M. Shefts, San Antonio, Pres.; Dr. John W. Middleton, 900 Strand, Galveston, Secy.

Texas Chapter, American Academy of Pediatrics, Fort Worth, April 11, 1960. Dr. J. T. Bennett, El Paso, Pres.; Dr. W. W. Kelton, 108 West 30th, Austin, Secy.

Texas Club of Internists. Dr. W. W. Bondurant, Jr., San Antonio, Pres.; Dr. T. Haynes Harvill, Medical Arts Building, Dallas 1, Secy.

Texas Dermatological Society, Fort Worth, April 11, 1960. Dr. Edmund N. Walsh, Fort Worth, Pres.; Dr. D. Shelton Blair, 1609 Medical Arts Building, Dallas, Secy.

Texas Diabetes Association, Fort Worth, April 10, 1960. Dr. Ralph Greenlee, Midland, Pres.; Dr. Warren W. Moorman, 901 W. Leuda, Fort Worth, Secy.

Texas Heart Association. Dr. Robert E. Leslie, El Campo, Pres.; Mr. Ernest T. Guy, 404 Jesse H. Jones Library Building, Houston 25, Executive Director.

Texas Hospital Association, Dallas, May 10-12, 1960. Mr. F. S. Walters, Jr., Amarillo, Pres.; Mr. O. Ray Hurst, 2208 Main, Dallas, Executive Director.

Texas Industrial Medical Association, Fort Worth, April 10, 1960. Dr. Max E. Johnson, San Antonio, Pres.; Dr. J. G. Burdick, P. O. Box 472, Pasadena, Secy.

Texas Neuropsychiatric Association, Fort Worth, April 10, 1960. Dr. Hamilton Ford, Galveston, Pres.; Dr. E. Ivan Bruce, 1014 Strand, Galveston, Secy.

Texas Ophthalmological Association, Fort Worth, April 11-12, 1960. Dr. Max Baldridge, Texarkana, Pres.; Dr. James H. Scruggs, 2223 Austin Ave., Waco, Secy.

Texas Orthopedic Association, Fort Worth, April 11, 1960. Dr. David M. Cameron, El Paso, Pres.; Dr. Margaret Watkins, 3503 Fairmount, Dallas, Secy.

Texas Otolaryngological Association, Fort Worth, April 12, 1960. Dr. Herbert H. Harris, Houston, Pres.; Dr. Louis E. Adin, 3707 Gaston, Dallas, Secy.

Texas Pediatric Society, October, 1960, Dallas. Dr. Byron York, Houston, Pres.; Dr. C. E. Gilmore, 811 Bonham, Paris, Secy.

Texas Physical Medicine and Rehabilitation Society, Fort Worth, April 12, 1960. Dr. Edward M. Krusen, Dallas, Pres.; Dr. Oscar Selke, Medical Professional Building, Houston, Secy.

Texas Proctologic Society, Dallas, February, 1960. Dr. Alvin Baldwin, Dallas, Pres.; Dr. H. Gray Carter, 915 St. Joseph St., Dallas, Secy.

Texas Public Health Association, Galveston, Feb. 22-24, 1960. Mr. Tom Warren, Austin, Pres.; Mr. Joseph N. Murphy, Jr., Box 4012, Austin 51, Executive Secy.

Texas Society of Anesthesiologists, Fort Worth, April 10, 1960. Dr. David O. Johnson, Austin, Pres.; Dr. M. T. Jenkins, Parkland Hospital, Dallas, Secy.

Texas Society of Athletic Team Physicians, Fort Worth, April 9, 1960. Dr. W. Harry Ledbetter, Wichita Falls, Pres.; Dr. Jack Brannon, 2715 Fannin, Houston, Secy.

Texas Society of Gastroenterologists and Proctologists, Fort Worth, April 10, 1960. Dr. Marcel Patterson, Galveston, Pres.; Dr. A. C. Broders, Jr., Scott and White Clinic, Temple, Secy.

Texas Society of Pathologists, Inc., Fort Worth, April, 1960. Dr. Jarrett Williams, Abilene, Pres.; Dr. Sylvia Johns, 414 Navarro St., San Antonio, Secy.

Texas Society of Plastic Surgeons, Fort Worth, April 9, 1960. Dr. Willard Schussler, El Paso, Pres.; Dr. Raymond Brauer, 6615 Travis, Houston, Secy.

Texas Society on Aging. Dr. Ernest W. Keil, Temple, Pres.; Mrs. William B. Ruggles, 3701 Stratford, Dallas, Secy.-Treas.

Texas Surgical Society, Fort Worth, April 3-5, 1960. Dr. Robert Wilson Crosthwait, Waco, Pres.; Dr. G. V. Brindley, Jr., Scott and White Clinic, Temple, Secy.

Texas Traumatic Surgical Society, Fort Worth, April 10, 1960. Dr. W. D. Marrs, Fort Worth, Pres.; Dr. W. E. Crump, 1300 8th St., Wichita Falls, Secy.

Texas Tuberculosis Association, Abilene, March, 1960. Mr. Zeb Rike, McAllen, Pres.; Miss Pansy Nichols, P. O. Box 6158, Austin 21, Executive Director.

District

First District Society. Dr. H. D. Garrett, El Paso, Pres.; Dr. E. S. Crossett, 1501 Arizona St., El Paso, Secy.

Second District Socity, Lamesa. Dr. Oscar E. Rhode, Colorado City, Pres.; Dr. John H. Chinn, Jr., Colorado City, Secy.

Third District Society, Lubbock, 1960. Dr. Grady M. Wallace, Lubbock, Pres.; Dr. H. Fred Johnson, 2308 W. Eighth, Amarillo, Secy.

Fourth District Society, San Angelo, May 16, 1959. Dr. W. L. Smith, San Angelo, Pres.; Dr. S. Braswell Locker, 1501 11th St., Brownwood, Secy.

Fifth and Sixth Districts Society, Corpus Christi, July 8-9, 1960. Dr. John W. Chriss, Pres.; Dr. James Gabbard, 1001 Louisiana, Corpus Christi, Secy.

Seventh District Society. Dr. Robert N. Snider, Austin, Pres.; Dr. Richard Lucas, 502 W. 13, Austin, Secy.

Eighth District Society, Corpus Christi, July 8-9, 1960. Dr. M. Warren Hardwick, Angleton, Pres.; Dr. J. L. Coleman, Box 3346, Victoria, Secy.

Ninth District Society, Brenham, March 17, 1960. Dr. Haden E. McKay, Humble, Pres.; Dr. Lyman C. Blair, 1212 Rothwell, Houston, Secy.

Tenth District Society, September, 1960. Dr. J. W. McCall, Jr., Beaumont, Pres.; Dr. Irving M. Richman, 3280 Fannin St., Beaumont, Secy.
Eleventh District Society. Dr. Ben Wilson, Tyler, Pres.; Dr. Phillip W. Taylor, 833 S. Beckham, Tyler, Secy.
Thirteenth District Society, Fort Worth, Fall, 1960. Dr. Frank S. Browne, Wichita Falls, Pres.; Dr. R. D. Moreton, 1217 W. Cannon, Fort Worth, Secy.
Fifteenth District Society. Dr. Charles Wise, Naples, Pres.; Dr. George Bennett, 402 S. Bolivar, Marshall, Secy.

Clinics

Dallas Southern Clinical Society Conference, Dalals, March 21-23, 1960. Dr. T. Taynes Harvill, Dallas, Pres.; Millard J. Heath, 433 Medical Arts Bldg., Dallas 1, Executive Officer.
New Orleans Graduate Medical Assembly, New Orleans, March 7-10, 1960. Dr. Ambrose H. Storck, New Orleans, Pres.; Mrs. Irma B. Sherwood, 430 Tulane Ave., New Orleans 12, Executive Secy.
North Texas-Southern Oklahoma Fall Clinical Conference. Dr. Frank J. Lee, 1300 8th, Wichita Falls, Chm.
Oklahoma City Clinical Society Conference, Oklahoma City, Oct. 24-26, 1960. Dr. Vernon D. Cushing, Oklahoma City, Pres.; Miss Alma F. O'Donnell, 503 Medical Arts Bldg., Oklahoma City 2, Executive Secy.
Postgraduate Medical Assembly of South Texas, Houston, July 18-20, 1960. Dr. C. Alsworth Calhoun, Houston, Pres.; Mrs. W. H. Dahme, 412 Jesse H. Jones Library Bldg., Houston 25, Exec. Secy.

Board Examinations

Texas State Board of Examiners in Basic Sciences. Henry B. Hardt, Ph.D., Fort Worth, Pres.; Mrs. Betty J. Anderson, Chief Clerk, State Office Bldg., 201 E. 14th St.

MEDICOLEGAL NOTES

Dispensing "Legend" Drugs Properly Calls for Knowledge of Patient

A recent case* concerning a physician who was prosecuted for violating provisions of the Food, Drug and Cosmetic Act which prohibit the dispensing of certain potentially harmful drugs without a prescription undoubtedly will be of interest to the physicians of Texas because of its potentially far-reaching effects. The case was decided by the United States Court of Appeals, Fifth Circuit.

The facts in the case disclosed that the physician involved on three separate occasions had sold to two federal agents, whom the physician supposed to be truck drivers, quantities of dextro-amphetamine hydrochloride tablets. The testimony in the case further disclosed that prior to dispensing these drugs the physician

> . . . had not prepared or given them any prescription and *had not physically examined either of them,* or "prescribed" a dosage *or otherwise attempted to acquaint himself with either the physical condition or needs of either man* . . . (emphasis supplied).

The jury in this case returned a verdict convicting the physician of the offense with which he had been charged, and upon appeal such conviction was affirmed. In affirming the trial court's decision the appellate court quoted language from another case similar in facts. Such language is quoted as follows:

> . . . If I came to you for treatment and *you, in your medical capacity examine me, and after examination* determine that certain barbiturates would be beneficial to me, then you have a right to write a prescription to me, and then I have a right to get them and use them, but not otherwise . . .

The Food, Drug, and Cosmetic Act passed by Congress several years ago regulates the handling, sale, and dispensing of certain drugs which are potentially harmful or dangerous unless used properly. These are the "legend" drugs which bear the label: "Caution: Federal law prohibits dispensing except upon prescription."

The decision in this case is important in that it is the first case to reach the appellate courts in which a physician had been charged with improperly dispensing this type of drug. Of even more interest to the physicians of Texas are certain comments by the court dealing with the issue of why this dispensing by the physician was in violation of this act.

There was no question or issue raised as to the physician's right to dispense these drugs to his patients—this was conceded. The main issue in this case was based upon the fact that the physician had not physically examined the patient or attempted to acquaint himself with the patient's condition or needs.

As a result of the holding in this case, physicians should be aware that the dispensing of "legend drugs" to a person without either examining the patient, attempting to acquaint himself with the patient's condition and needs, or being aware of the patient's condition as a result of past treatment of the patient may well constitute a violation of the Food, Drug, and Cosmetic Act.

—PHILIP R. OVERTON, LL.B., Austin.

**Brown v. United States (250 F. 2d 745).*

EDUCATION

Texas Postgraduate School To Sponsor Five Courses

The University of Texas Postgraduate School of Medicine is sponsoring postgraduate courses on various subjects during the months of January and February to be held at the Texas Medical Center in Houston.

The following courses will be offered: "Physical and Medical Aspects of Radioisotope Use," January 4-29; "Internal Medicine," January 5-May 17; "Clinical Psychiatry," January 26-May 3 (the course will be held each Tuesday evening, January 26-May 3 and each Thursday evening, January 28-May 5); "Radiological Physics," February 1-March 25; and "Gastroenterology," February 25-27.

For further information concerning the courses, those interested may write the University of Texas Postgraduate School of Medicine, Texas Medical Center, Houston 25.

Postgraduate Courses

Respiro Cardiac Resuscitation, New York, February 4-5.—The National Resuscitation Society will present an intensive week end course in respiro cardiac resuscitation under the sponsorship of the American College of Cardiology. Matriculation fee is $75. For additional information, those interested may write to the Secretary, National Resuscitation Society, Inc., 2 East 63 Street, New York 21.

Rhinology, Chicago, February 10-13.—A seminar in "Reconstructive Surgery of the Nasal Septum and External Nasal Pyramid" will be held in New Orleans, February 10-13, under the auspices of the Department of Otolaryngology, Louisiana State University Medical School, and the

Charity Hospital. The American Rhinologic Society will cooperate in the presentation. For further information, those interested may write to Dr. Robert M. Hansen, 1735 North Wheeler Avenue, Portland 12, Oregon.

Pediatrics, Galveston, February 11-13.—The University of Texas Medical Branch will present a postgraduate course in pediatrics in Galveston, February 11-13. The postgraduate course has a 15 hour credit rating for members of the Texas Academy of General Practice. Tuition fee is $15.

Guest speakers are as follows: Dr. Arild E. Hansen, Oakland, Calif.; Dr. J. Roswell Gallagher, Boston; Dr. Jack Metcoff, Chicago; Dr. Virginia Apgar, New York; and Dr. Alex Steigman, Louisville, Ky. Those desiring further information may write Dr. Arr Nell Boelsche, Assistant Professor of Pediatrics, University of Texas Medical Branch, Galveston.

Mass Casualties, San Antonio, February 15-19.—A course in the management of mass casualties will be offered to civilian physicians by the Army Medical Center at Fort Sam Houston, San Antonio, February 15-19. There is only one space available in the quota set up for the course. Those interested may write the AMA Council on National Defense, 535 North Dearborn, Chicago 10, which set the quota for the course.

Baylor Medical School Announces Taub Award in Psoriasis

The annual Mr. and Mrs. J. M. Taub International Memorial Award for Psoriasis Research of $1,000 will be offered this year by the Department of Dermatology at Baylor University College of Medicine, Houston. It was established in 1957 by Carol and Henry Taub in honor of their grandparents.

The award is designed for the individual or group who has done the "most outstanding investigative work" in the field of psoriasis. Results of the research must have been presented before a dermatological medical society or published in one of the recognized medical journals during the calendar year.

The name of any applicant for the award, together with supporting data, should be submitted for consideration by December 31 to Dr. John M. Knox, Department of Dermatology, Baylor University College of Medicine, Houston 25.

M. D. Anderson Staff Receives Cancer Grants

The National Cancer Institute of the United States Public Health Service has announced recently the award of eight research grants to staff members of the University of Texas M. D. Anderson Hospital and Tumor Institute in Houston. The grants total $140,758.

Among those receiving the grants were Daniel Billen, microbiologist, who received $14,381 for an investigation of the potentialities of hemic cells in irradiated mice, and L. Dmochowski, virologist, A. C. Griffin, biochemist, and R. B. Hurlbert, assistant biochemist, who received $17,538 for purification of the mammary tumor-induction agent in mice.

Others include V. M. Doctor, associate biochemist, and C. C. Shullenberger, R. S. Nelson, and D. E. Bergsagel, associate internists, who received $7,112 for studies of the metabolism of vitamin B_{12} in relation to cancer; F. L. Haas, biologist, who received $31,428 for training of graduate students in research on the biology of growth processes; Dr. Haas and David E. Anderson, associate biologist, who received $14,490 for investigation of the genetic aspects of bovine ocular carcinoma; Bruno Jirgensons, biochemist, who received $9,472 for studies to characterize plasma and urinary proteins; Dr. William O. Russell, pathologist, who received $29,814 for histochemical research in community cancer diagnosis; and Dr. Russell and Dr. Felix Rutledge, gynecologist, who received $16,523 for investigation of the effects of irradiation on cervical carcinoma and normal vaginal cells (cytologic and histochemical studies of exfoliated cells).

DRUG NOTES

Drug from Fig Tree Suggested for Burns

DEBRICIN (Johnson & Johnson) is a lyophilized protein splitting enzyme derived from a variety of the fig tree, Ficus Protease. It is under clinical investigation and not available at this writing. The agent, which is specific in its activity, lyses denatured collagen, but does not affect partially denatured nor living tissue. Debricin is suggested as an excellent agent for the debridement of deep second and third degree burns or in other conditions where it is necessary to remove devitalized tissue without affecting the intact areas.

It is said to exert a marked but highly selective action on fibrin and denatured elastin and collagen substrates. It readily cleans a wound of necrotic tissue and liquefies thick exudate. Debricin is suggested in the treatment of burns, ulcerative lesions, wound infections, and infected sinus tracts and may be of possible use in empyema.

Debricin is said to be essentially without local and systemic toxicity even when applied to large injured areas. It has produced irritation and even corneal perforation in the eyes of rabbits when the pure powder was dusted into the eye. However, prompt irrigation greatly reduced the irritation and permanent damage was avoided.

The new drug cannot be given intravenously, intraperitoneally, intramuscularly, or subcutaneously. Orally it is nontoxic and topically shows no local irritation nor systemic toxicity.

The drug is a tan stable powder that has been precipitated from the sap of the fig tree, purified by dialysis, lyophilized, and sterilized. It probably will be available as a sterile packet of the dry material to be reconstituted into a sterile buffered vegetable gum or suspended in the sterile buffered base diluted with saline solution.

Debricin is inactivated by quaternary ammonium salts, hexachlorophene, soaps, and oxidizing agents. Generally the function of the tetracylines is impaired, and they also impair the activity of the enzyme. Neomycin, bacitracin, chloramphenicol, and penicillin are compatible. Topical antibiotics, simultaneously, however, are not recommended at this time. It is said that the cleansing action of Debricin is faster than Varidase (Lederle) and Trypsin (Parenzyme —National, Tryptar—Armour).

MICRIDIUM (phenacridane chloride, Johnson & Johnson) has had clinical trial against a number of antibiotic resistant staphylococci. The compound is said to be bacteriostatic in extremely high dilution against both gram-positive and gram-negative organisms. The compound is yellow in color and water soluble and forms a stable solution. It can be buffered conveniently to a pH of 6.5. The material also inhibits the growth of certain fungi. Significantly, a

1:10,000 concentration kills Pseudomonas aeruginosa in 15 minutes or less.

Basically the substance is a derivative of the antiseptic dye acridine. It is related faintly to quinacrine (Atabrine—Winthrop) and to the cationic agents or surface active agents such as the quaternary ammonium compounds. Thus, the compound is similar in its type of action to benzalkonium chloride (Zephiran—Winthrop) and benzethonium chloride (Phemerol—Parke-Davis).

A theory has been postulated that the acridine dyes function by being quaternized in vivo to quaternary ammonium compounds. Here in this compound is the proposed quaternary compound already prepared. This is true also in the case of acriflavine.

The material is suggested for use in the topical treatment of superficial bacterial infections. Company literature also claims a low order of toxicity.

The Upjohn Company is working on two new antibiotics: FERVENULIN, which may be useful as an antitrichomonal drug, and STREPTOZOTOCIN, which appears to be relatively wide range.

Fervenulin has been isolated from a California soil sample and is the product of an actinomycete. The compound has been active against at least 23 types of bacteria and inhibitory toward 16 different types of fungi. In hamsters and mice 50 per cent cures have been obtained against trichomonas infection.

Streptozotocin is said to have good antibacterial activity against micrococci, diplococci, enterococci, Pasteurella, Salmonella, and Proteus. It has no cross-resistance with 10 of the common, commercially available antibiotics.

VONTIL (Smith Kline and French) is an antiemetic, still under investigation and not yet available. The new substances is a phenothiazine derivative, closely related to Compazine and Stelazine (Smith Kline and French). Vontil differs from Compazine in that a dimethyl sulfonamide group replaces the halogen of the Compazine phenothiazine nucleus. It replaces $-CF_3$ in the same position of Stelazine.

The drug may be of use in nausea and vomiting caused by toxicosis, drugs, malignant neoplasms, infections, postoperative states, pregnancy, and motion sickness. Good to excellent relief has been obtained in about 86 per cent of the patients.

It is said that Vontil may be the most potent antiemetic yet tested; also that effective doses give a minimum of side reactions. The most common side effect was mild sedation in about 10 to 12 per cent of the patients. Other side effects were stimulation, tachycardia, hypotension, tremors, facial spasm, muscular weakness, and gastrointestinal upset. These occurred in less than 3 per cent of the patients.

In hexobarbital potentiation Vontil was about one-twentieth the potency of Thorazine and about one-third the potency of Compazine. The adult oral dose is about 0.25 mg. to 1.0 mg., three or four times a day depending on the severity of the case. The dose needed will seldom be over 3.0 mg. in 24 hours. Intramuscular injections of 0.25 mg. to 0.5 mg. may be given 3 or 4 times a day. A second injection may be given within an hour following initial administration if needed; subsequent doses should not be given more frequently than once every 4 to 6 hours.

The drug may be given intravenously if diluted with 5 per cent glucose or normal saline solution. The dose will be about 0.5 mg., to be repeated if necessary. The dose may be injected into the tubing of an intravenous drip apparatus near the point of venipuncture.

The dosage for children orally is based on about 0.01 mg. per 5 pounds of body weight and may be repeated three or four times a day. Rectally, suppositories of 0.2 mg. may be cut in half for children of 20 to 25 pounds, to be given every 6 hours. Parenterally, for children the dose should be cut to about 0.005 mg. for each 5 pounds of body weight, every 6 hours if needed. Oral administration should be resumed as soon as possible. Intravenous administration is not recommended for children at this time. The adult dose forms available probably will be tablets of 0.25 mg. and 0.5 mg., ampules of 1 cc. containing 0.5 mg., and suppositories of 0.8 mg. and 1.0 mg. For children, pediatric drops of 0.01 mg. per drop, ampules; 2 cc. with 0.5 mg. per milliliter, and suppositories of 0.2 mg. and 0.4 mg. strength.

For more complete information as to dosage, contraindications, and side effects the company literature may be consulted when the product becomes available.

Schering Corporation recently announced a 20 per cent reduction in its price for its new antifungal antibiotic, FULVICIN.

—HERBERT SCHWARTZ, M.S., Austin.

MEDICAL MEETINGS

Cancer Symposium to Be Held February 25-27 in Houston

"Cell Physiology of Neoplasia" will be the subject of the fourteenth annual Symposium on Fundamental Cancer Research which will be held February 25-27 in Houston at the University of Txeas M. D. Anderson Hospital and Tumor Institute.

Co-sponsors of the symposium include the University of Texas Postgraduate School of Medicine, the American Cancer Society, Texas Division, and the Texas State Department of Health.

Among the topics to be presented will be fundamental aspects of genetics in carcinogenesis, gene interaction in neoplastic growth, genetic basis of cell resistance, and heredity and human cancer.

A social hour and dinner will be held Friday, February 27. For advance registration materials and further information, doctors may write the Symposium Chairman, University of Texas M. D. Anderson Hospital, Texas Medical Center, Houston 25. All physicians are welcome to attend.

Urological Society To Meet in Waco

A meeting of the Texas Urological Society will be held January 23-24 in Waco. It is open to all interested physicians.

Four guest speakers will highlight the program. They include Dr. O. S. Culp, Rochester, Minn., who will speak on "Heminephro-Ureterectomy: A Comparison of One Stage and Two Stage Operations," and "Cryptorchism: Experiences During the Past 9 Years"; Dr. Samuel L. Raines, Memphis, Tenn., "Urethritis in the Female," and "Trauma of the Urinary Tract"; Dr. T. Leon Howard, Denver, "Renal Vicissitudes"; and Dr. John R. Derrick, "Vascular Variations in Renal Hypertension."

Dinner and dancing will be held at the Ridgewood Country Club, Saturday evening, January 23.

Dr. M. A. Magid, Waco, is serving as program chairman for the meeting. Those interested in attending are asked to notify Dr. Magid at 1525 Colcord in Waco.

Texas Radiological Society To Meet in Houston

The forty-seventh annual meeting of the Texas Radiological Society will be held January 22-23 at the Shamrock-Hilton Hotel in Houston. All physicians are welcome to attend.

Guest speakers will be Dr. John A. Evans, professor of radiology, Cornell Medical College, New York; Dr. Bernard S. Wolf, chief radiologist, Mt. Sinai Hospital, New York; Dr. Theodore P. Eberhard, radiologist, St. Joseph Mercy Hospital, Ann Arbor, Mich.; Dr. Stanley M. Wyman, professor of radiology, Harvard Medical School, Boston; Dr. Bernard S. Epstein, chief radiologist, Long Island Jewish Hospital, New Hyde Park, N.Y.

Among the subjects to be on the program are nephrotomography in the differentiation of renal cyst and tumor, small hiatal hernia, problems in the management of cancer of the breast, peri-ureteral fibrosis, radiographic diagnosis of pituitary adenomas with special reference to body section examinations, carcinoma of the pancreas, some unusual radiographic features, segmental colitis, the treatment of carcinomas of the skin, dissecting aneurysm of the thoracic aorta, myelographic changes associated with painful conditions of the cervical and lumbar spine other than herniated disks, web and weblike lesions of the esophagus, benign tumors of the colon, and considerations in the radiation of benign conditions.

There will be a cocktail party and annual banquet the evening of January 22. A coffee and dutch treat luncheon are being planned for the ladies.

Registration fee for nonmembers of the society is $20 and for radiological residents and military personnel, $5. For further information, doctors may write Dr. R. P. O'Bannon, 650 Fifth Avenue, Fort Worth.

San Antonio Readies Program

With 17 guest speakers, technical exhibits, a dinner dance, friendship party, and ladies' entertainment, the International Medical Assembly of Southwest Texas is ready to get under way with its annual program January 25-27 in San Antonio. Immediately preceding will be two one-day seminars sponsored by the San Antonio Division of the Post Graduate School of Medicine of the University of Texas.

A registration fee of $20 (which may be sent in advance to the Assembly, 202 W. French Place, San Antonio) will cover all activities.

Fields of practice and speakers among the guests are the following: anesthesiology, Dr. Harvey C. Slocum, Washington, D.C.; dermatology, Dr. Louis A. Brunsting, Rochester, Minn.; endocrinology, Dr. Laurance W. Kinsell, Oakland, Calif.; gastroenterology, Dr. Bernardo Sepulveda, Mexico, D.F.; internal medicine, Drs. William S. Middleton, Washington, D.C., and Louis G. Welt, Chapel Hill, N.C.; neurology, Dr. Russell N. De Jong, Ann Arbor, Mich.; ophthalmology, Dr. Peter C. Kronfeld, Chicago; obstetrics-gynecology, Dr. Herbert E. Schmitz, Chicago; pathology, Dr. Leopold G. Koss, New York.

Also included are pediatrics, Dr. Alexander S. Nadas, Boston; psychiatry, Dr. Harold Rosen, Baltimore; radiology, Dr. John D. Reeves, Gainesville, Fla.; surgery, Drs. Wiley F. Barker, Los Angeles; Wilfred G. Bigelow, Toronto, Canada; Robert W. Buxton, Baltimore; and John M. Waugh, Rochester, Minn.

Seminar on Glaucoma Set January 23 in San Antonio

A seminar on glaucoma will be presented by the University of Texas Postgraduate School of Medicine, San Antonio Division, January 23, in the Robert B. Green Memorial Hospital, San Antonio. The seminar will precede the International Medical Assembly of Southwest Texas, January 25-27 in San Antonio.

Among the topics to be discussed at the symposium are the following: "The Pathology and Physiology of Glaucomas"; "The Office Diagnosis of the Primary Glaucomas"; "Combination of Simple and Angle-Closure Glaucoma"; "Practical Value of Tonography"; "The Surgical Treatment of Congenital Glaucoma: Current Techniques"; and "A Critical Comparison of Corneo-Sclerotomy and Iris Inclusion Operations."

Faculty members of the postgraduate school to participate on the program will be Major General Elbert DeCoursey, director, Southwest Foundation for Research and Education, San Antonio; Dr. Wendell Gingrich, associate professor of ophthalmology, University of Texas Medical Branch, Galveston; Dr. Peter C. Kronfeld, professor of ophthalmology, University of Illinois, Chicago; Dr. James L. Mims, Jr., clinical lecturer in ophthalmology, San Antonio Division, University of Texas Postgraduate School of Medicine, San Antonio; and Dr. Gaynelle Robertson, professor of ophthalmology, University of Texas Medical Branch, Galveston.

All interested physicians are invited to attend; tuition is $15. For additional information concerning the symposium, doctors may write to Dr. Herman S. Wigodsky, director of the San Antonio Division, University of Texas Postgraduate School of Medicine, San Antonio.

Texas Pharmacy Law Reviewed in Austin

Forty-nine doctors, pharmacists, executive secretaries, nurses, lawyers, wholesalers, manufacturers, hospital representatives, and teachers of pharmacy met in Austin to study the Texas Dangerous Drug Law and the Amended Texas Pharmacy Law, November 13.

Pat Bailey of Austin, assistant general counsel for the Texas Medical Association, reviewed the laws. A question and answer period followed, conducted by Mr. Bailey. The various representatives were to report the information to their respective organizations.

The Texas Pharmaceutical Association was host at a buffet dinner preceding the program.

Texas Physicians Participate In Miami Dermatological Meet

Several Texas doctors are participating in the international symposium on "Griseofulvin and Dermatomycoses," October 26-27, at Miami, sponsored by the University of Miami's Department of Medicine, Division of Dermatology.

These physicians include Dr. John Ferguson, Fort Sam Houston; Dr. John M. Knox, Houston; Dr. C. H. McCuistion, Austin; Dr. J. Fred Mullins, Galveston; Dr. J. Lewis Pipkin, San Antonio; and Dr. George Prazak, Fort Sam Houston.

OF GENERAL INTEREST

Personals

Dr. Robert D. Moreton of Fort Worth has been named to a special ad hoc advisory committee to the American Cancer Society. Dr. Moreton represents the American College of Radiology on this committee, which is made up of representatives of professional societies to advise the American Cancer Society on planning and implementing the society's educational program.

Dr. M. H. Crabb, Fort Worth, secretary of the Texas State Board of Medical Examiners, was elected to a second term as a member at large of the National Board of Medical Examiners.

Dr. Hugo T. Engelhardt of Houston has been appointed by the American Diabetes Association as governor of Texas for the organization for a 3 year term.

Dr. J. B. Heath, Madisonville, was reelected one of the University of Texas Dads' Association vice-presidents, November 7, in Austin at the twelfth annual Dads' Day celebration. *Dr. C. M. Phillips,* Levelland, completed his term as president at this time.

The Downtown Harlingen Kiwanis Club recently honored *Dr. Thomas J. LaMotte,* Harlingen, for donating his time free of charge in performing tonsillectomies on needy children. During the past 3 years, he has performed 50 of these operations.

The following El Paso doctors have had births in their families: A girl for *Dr. and Mrs. John L. Lukowski,* born October 2; a boy for *Dr. and Mrs. Irvin J. Goldfarb,* born October 3; and a girl for *Dr. and Mrs. Francisco Licon,* born November 6.

Dr. W. Compere Basom, El Paso, spoke at the annual meeting of the American Fracture Association, November 1-3 in New Orleans, as well as presiding at a noon luncheon and moderating a morning session.

Board of Obstetrics and Gynecology To Hold Examinations in January

The American Board of Obstetrics and Gynecology part I examinations will be held in various parts of the United States and Canada on January 16, 1960.

Candidates notified of their eligibility to participate in part I must submit their case abstracts within 30 days of notification of eligibility. No candidate may take the written examination unless the case abstracts have been received in the office of the secretary.

Current bulletins outlining present requirements may be obtained by writing to the secretary's office: Dr. Robert L. Faulkner, American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

Chest Physicians Announce Contest

Undergraduate medical students are encouraged to enter the 1960 Essay Contest of the American College of Chest Physicians by submitting manuscripts on any subject relating to the diagnosis or treatment of chest diseases (heart or lungs) by April 1, 1960.

Three Baylor University College of Medicine students were second place winners in the 1959 competition. L. O. Baum, J. A. Murray, and N. H. Oldham brought the second prize to Houston with a paper entitled "Evaluation of Lung Volumes and Intrapulmonary Gas Mixing in Diseased and Normal Children."

Three cash awards are given to winners by the college. First prize is $500; second prize, $300; and third prize, $200. Since the contests were initiated in 1950, the Committee on College Essay has distributed $6,600 to students writing the award-winning essays.

Copies of the details of the contest are being sent to deans of medical schools throughout the world, and presidents of medical fraternities and sororities. For further information, those interested may write the American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Ill.

Physicians' Status With Selective Service

All hospitals and schools utilizing residents should be aware of the fact that the physicians concerned may be ordered for military service during residency training if a call for physicians is placed upon Selective Service, according to Col. Morris S. Schwartz, state director for Selective Service.

Current Selective Service directives inform (1) that a physician should not be placed in Class II-A to complete residency training unless in the opinion of the local board his services are absolutely essential to the operation of the hospital or he is a participant in a residency training program of the Armed Forces or Public Health Service, and (2) that all other physicians who are not veterans may be ordered to report for induction if a call for physicians is placed upon the Selective Service System during their residency training.

For further information on the Selective Service program, doctors may write to Colonel Schwartz, Selective Service System, 304 East Fifth Street, Austin 14.

Directors of Cancer Institutes Form New Organization

The directors of cancer research institutes in America have formed an organization, the Association of Cancer Institute Directors, for the purpose of exchanging information among the various institutes.

The organization is composed of the senior scientific executives of those institutions and autonomous divisions and departments whose principal activities are concerned with the study of malignant disease and the treatment of cancer patients. Dr. R. Lee Clark, Jr., Houston, director and surgeon-in-chief, University of Texas M. D. Anderson Hospital and Tumor Institute, was elected secretary-treasurer of the organization.

The association has been designed to support investigations of the causes, nature, treatment, and prevention of malignant diseases; to encourage the exchange of ideas, information, personnel, and special facilities between groups with predominant interests in cancer; to foster educational opportunities in the biomedical sciences; to provide guidance to private and civil organizations concerning cancer research, education, and the care of cancer patients; and to expedite the dissemination of information by the meeting together of the scientific executive officers of cancer institutes.

Poison Control Centers Located in Eight Cities

Poison control centers in eight cities in Texas now are offering poison information service. The centers are located in Abilene, Austin, Corpus Christi, Dallas, Fort Worth, Galveston, Houston, and Tyler.

The poison information facilities are available to all physicians and personnel of hospitals, emergency rooms, and allied medical sciences.

Criteria for a functional poison control center include supervision of services 24 hours a day by a physician, availability of informational services for responses by a center's physician to inquiries by physicians only and treatment at the center for patients who come or are brought in, an adequate reference library for immediate study on toxic materials usually causing poisoning, a center with all emergency drugs, and a signature and submission to the State Department of Health of information and agreement concerning the control center.

Those desiring further information may write to Director of the Division of Occupational Health, State of Texas Department of Health, Austin.

The addresses and phone numbers of the Texas poison control centers follow:

Abilene	Hendrick Hospital Emergency Room, Fifth Floor	ORchard 4-3551 ORchard 4-8635
Austin	Brackenridge Hospital, Emergency Room, 14th and Sabine Streets	GReenwood 8-8571, Extension 220, Extension 240
Corpus Christi	Memorial Hospital, Medical Library, 2606 Hospital	TUlip 4-2411
Dallas	Parkland Memorial Hospital Poison Information Center Emergency Operating Room	LAkeside 6-7611, Extension 402 Extension 425
Fort Worth	W. I. Cook Memorial Hospital for Children, 1212 West Lancaster Avenue	EDison 6-5521, Extension 64
Galveston	Galveston Poison Control	SOuthfield 5-5541, Extension 596 or "Poison Information"
Houston	Gulf Coast Poison Information Center, Middle Building, Wolff Memorial Home, 1300 Kenwood	JAckson 6-3731
Tyler	East Texas Poison Control Center: 2817 Fry Medical Center Hospital Emergency Room 416½ North Bois d'Arc	LYric 3-0531 LYric 4-9361 LYric 4-6651, Extension 44

Gulf of Mexico, Salt Mines Said Safe for Dumping Atom Waste

Texas' greatest salt mines, as well as the Gulf of Mexico, may some day become safe dumping grounds for radioactive waste, experts told the Texas Committee on Atomic Energy at the October 2 meeting of the committee held in Dallas.

"It all boils down," said Dr. Warren K. Sinclair of the M. D. Anderson Hospital and Tumor Institute, Houston, "to public opinion and fear outweighing logic and findings."

"Thousands of curies are safely being disposed of off New England, and the amount of waste being dumped is not sufficient to cause any harm as far as science now knows," he said.

He added that the public bugaboo of the horrors of radiation strike the politician so that he is almost forced to overlook facts.

Texas salt mines might become burial vaults for these otherwise dangerous materials, according to W. B. Heroy of the Geotechnical Corporation in Dallas and a member of the committees studying the disposal problem.

Charles R. Borden of the State Health Department added the following comment of caution concerning the dumping: "We don't mean to say unlimited dumping is safe. But in these low level amounts and carefully regulated by the proper authorities we can see no impending dangers."

Society of Nuclear Medicine To Publish Quarterly Journal

The Society of Nuclear Medicine has announced the forthcoming publication of its official organ, *The Journal of Nuclear Medicine.* The first quarterly issue will appear during the month of January, 1960.

Editor of the journal will be Dr. George E. Thoma of St. Louis. The editorial content of the publication will be directed towards those members of the medical and allied professions who are interested in the diagnostic and therapeutic application of radioisotopes and in human radiobiology. Annual subscription rate is $10.

Additional information concerning the journal may be obtained by writing the editor at Southwest Medical Center, 3915 Watson Road, St. Louis 9.

Tuberculosis and Public Health

The notification to the local health authority that a case of communicable disease exists within the particular jurisdiction is the first step toward control. The reporting of cases of tuberculosis by physicians in Texas has been required through statutory regulation for almost a half century. The number of cases of tuberculosis has not varied markedly in the past 25 years, varying between 2,500 and 3,500 cases per year. This type of reporting of tuberculosis occurred even when the annual deaths from tuberculosis in the state exceeded the reported cases by almost two to one.

When a physician reports a case and the immediate problem of treatment and hospitalization has been completed, an important step is to determine the source of the patient's infection. This can be a difficult or a simple matter in some cases. In general, the local health department can be of great assistance in interviewing and collecting the contacts of the patient for study. In the contact examination, another important feature can be locating those people who have been infected by the reported case. With a somewhat limited reduction in the tuberculosis problem, this epidemiological approach and study of cases is taking on more significance and probably will become the backbone of future control programs. If the reported case is of an infectious character, it provides the physician or local health department with information so that proper protection can be provided contacts if protection is needed. Frequently, circumstances are such that infectious cases cannot be removed from the environment immediately, and for the protection of children especially, early precautions are mandatory.

Tuberculosis patients are notorious for moving from one area to another, changing physicians, and neglecting to take treatment. When a case has been reported to the health department, the mechanism is available for providing continuity of supervision through the health department nursing staff for home visiting and conferences directed toward getting the patient under medical supervision if it is needed by the patient. Unless physicians, clinics, and hospitals report the cases of tuberculosis, there is no way of determining the frequency of the disease and the magnitude of the problem. Without this information, it is impossible to plan for an adequate control program. Where physicians do an excellent job of reporting, then the information can be used to determine the efficiency of the control program. In other words, it provides a definite yardstick of measurement because it can be evaluated against similar countries and states.

In reporting cases of tuberculosis, the physician will have the assistance of the health department in maintaining supervision and treatment of the individual cases. It is to the patient's advantage that the case be reported; then he can be assured of better treatment. It is helpful to the community so that proper protection of its citizens can be maintained. An adequate and complete control program can be initiated only through the reporting of the disease.

—Committee on Tuberculosis,
Texas Medical Association.

Great Men of Padua

Upon examining the history of the world it is interesting that each historian has written that he was living in the "golden age" of the universe.

Professor Breasted, the Egyptologist, thinks that the twenty-ninth century before Christ was the greatest. This was the time that Djoser or Neter-khet, first king of the third dynasty, was buried under an enormous pyramid of masonry, nearly 400 feet square and over 250 feet high. Under the pyramid Djoser's builders excavated a shaft 80 feet deep, with a granite lined burial chamber at the bottom. The granite was brought by river from Aswan, nearly 700 miles away. This was the first pyramid and the oldest large stone building in the world.

Thus, out of the ocean of oblivion man had emerged in a highly civilized state on the banks of the Nile. How was this miracle achieved, for everything before had been built of mud and wood? The answer probably is that, as at other crises in human history, the hour brought forth the man. From the mists of legend and fragmentary history which surround this remote epoch, one figure looms up: we know his name—Imhotep (he who comes in peace).

Twenty-five centuries after Imhotep's death, the historian Manetho transmitted to us one scrap of information: "In Djoser's reign lived Imhotep who because of his medical skill had the reputation of Aesculapius and was the inventor of the art of building in hewn stone. He also paid attention to writing." Imhotep was deified, and many bronze statues of him exist today along with the great step pyramid which he built.

Dr. Paul Shorey thinks that the fifth century before Christ was the greatest. This was, of course, the time of Hippocrates, who gave us the first scientific approach to medicine along with the "Oath" which has held our group together down to the present time. This was indeed a great century.

Dr. J. J. Walsh puts none above the thirteenth century A. D., and many in whom the spirit of the renaissance has entered contend that the palm and the laurel go to the "quattrocento." There are reasons for choosing almost any other century, but this will give an idea of how some people feel.

The great Sir William Osler writing in 1901 said, "For countless generations the prophets and kings of humanity have desired to see the things which men have seen, and to hear the things which men have heard in the course of the wonderful nineteenth century. To us in the medical profession, who deal with this unit, and measure progress by the law of the greatest happiness to the greatest number, to us whose work is with the sick and suffering, the great boon of this wonderful century, with which no other can be compared, is the fact that the leaves of the tree of science have been for the healing of the nations." I wonder what Sir William would write in 1959.

To my mind, the greatest century for the healing arts is the sixteenth century A. D. and centers around a group of medical men at "Fair Padua, Nursery of the Arts." The beginning of the sixteenth century (just after the discovery of America by Columbus and when Leonardo da Vinci was creating his masterpieces) is heralded at Padua by the pro-

fessor of medicine Peter of Abano, the Great Conciliator. He is the first in a line of distinguished physicians connected with the great school of Padua. He is known as "the Conciliator" from his attempt to reconcile the diverse views of philosophy and medicine. He had an extraordinary reputation as a practitioner and author. The early editions of his texts are among the most superb works ever printed.

The second in line of these great physicians was Andreas Vesalius of Brussels. This professor of anatomy at Padua in his book, "The Fabric of the Human Body," published in 1543, gave us the first scientific anatomy and the greatest medical book ever printed. This book has been literally "thumbed to death" by use during the centuries, and good copies are hard to come by these days. But it still remains a scientific masterpiece and with its beautiful woodcuts a thing of aesthetic beauty. It was, of course, Andreas Vesalius that broke away from the 15 century old fallacies of Galen.

I would say in defense of possible progressive thinkers of that time that science was considered by the church holy so that if people broke away from the old line of scientific thought, they were in danger of being labeled heretics, which meant burning at the stake. Galileo, a contemporary professor at Padua, "got scorched a little" for feeling that the earth revolved around the sun. The reason that Padua was such a great university was the fact that it consisted of a group of free thinking students working with a liberal minded faculty that was not harassed by the church. Such is of what great discoveries are made. It is sad that poor Vesalius became so disgusted with his critics following the publication of his book that when still a young man, he left the university, went to Spain to become court physician to Charles V, and disappeared into oblivion. He died when shipwrecked onto the Greek island of Zante in 1564.

The successor to the chair of anatomy at Padua following Vesalius was the great Realdo Columbus, who very clearly and independently described the lesser or pulmonic circulation. He showed that the blood passes from the right ventricle into the pulmonary artery and through the lungs into the pulmonary vein and, thence, into the left auricle. He was preceded in this discovery by Michael Servetus, who was burned at the stake in Geneva for his heretical feelings about the Holy Trinity, but the fact remains that Columbus preceded Harvey by at least 60 years. Following Columbus in the chair of anatomy at Padua was another famous man, Gabriele Falloppio, who did not make as shattering discoveries as his predecessors but certainly left his name on one of the most important organs in the human body.

Following Falloppio was Fabricius ab Aquapendente, the teacher of William Harvey. This man had the discovery of the circulation within his grasp but was blind to what he saw. He taught Harvey about the valves in the veins (which Harvey later told Boyle was what made him discover the circulation of the blood). Fabricius was truly a worthy follower assuming the professorate in 1565. He was professor of anatomy at Padua for a long time, and in the thirtieth year of his teaching, after asking the board of the University many times for the money to build an anatomical amphitheater, he disgustedly built at his own expense the beautiful but small anatomical theater which still exists in the University buildings at Padua.

Harvey came to Padua about 1598 and was taught anatomy by Fabricius. He went back to England in 1602. Harvey's stemma can still be seen on the walls of the university. Harvey, with the training of the best anatomist of his day, went back to London to perform the greatest piece of experimental deductive reasoning that the world has ever known. Sir Thomas Browne, who had the highest veneration for Harvey, wrote ". . . his piece, De Circul. Sang., which discovery I prefer to that of Christopher Columbus."

Harvey's little treatise is the second greatest medical book ever printed and for which he suffered great criticism from his colleagues. The experimental method belongs to Harvey and not to John Hunter.

The sixteenth century A. D. represents a flowering of truth, beginning with a small group of liberal minded students thought of as progressive, nurtured by a tolerant faculty, and blossoming into the greatest discoveries the history of medicine has ever known. This was truly a remarkable century.

—William M. Crawford, M.D., Fort Worth.

Gifts to the Library

Dr. L. L. Stephens, Robstown, 980 journals.
Dr. Nelson L. Schiller, Austin, 50 journals.
Dr. B. O. White, Austin, 17 journals.
Dr. Morris Davidson, Austin, 28 journals.
Kahn Memorial Hospital, Marshall, 185 journals.
Dr. T. P. Moriarty, Austin, 15 books.
Dr. L. E. Hamilton, Rogers, 98 journals and 8 books.
Dr. Maurice Jacobs, Austin, 8 journals.
Dr. Robert Rothen, Austin, 4 journals.
Dr. Walter D. Roberts, Austin, 38 journals and 7 books.
Dr. Henry Hilgartner, Austin, 50 journals.
Dr. Sterling Hardt, Bastrop, 108 journals and 1 book.
Dr. Robert G. McCorkle, Austin, 1 book.
Dr. Henry W. Newman, Austin, 34 journals.
Dr. Robert Loveless, Bastrop, 129 journals and 1 book.
Dr. James W. Boyle, Austin, 23 journals.

★ Books

Books Newly Acquired

American Medical Association, Officials Actions 1846-1958, Chicago, American Medical Association, 1959.

Belisario, John C.: *Cancer of the Skin,* London, Butterworth, 1959.

Brody, Morris W.: *Observations on Direct Analysis, The Therapeutic Technique of Dr. John N. Rosen,* New York, Vantage Press, 1959.

Burgess, Perry: *Who Walk Alone,* New York, Henry Holt, 1940.

Busch, Harris: *Chemistry of Pancreatic Diseases,* Springfield, Ill., Charles C Thomas, 1959.

Ciba Collection of Medical Illustrations: *Digestive System, Digestive Tract,* pt. 1, Upper Digestive Tract, New York, Ciba, 1959.

Ciba Foundation: *Pain and Itch: Nervous Mechanisms . . .* , Boston, Little, Brown and Co., Ciba Foundation Study Groups, 1959.

Ciba Foundation: *Steric Course of Microbiological Reactions,* Boston, Little, Brown and Co., Ciba Foundation Study Group, 1959.

Corner, George W.: *Attaining Manhood,* ed. 2, New York, Harper and Brothers, 1957.

Corner, George W.: *Attaining Womanhood,* ed. 2, New York, Harper and Brothers, 1957.

Friedman, Arnold P., and Merritt, H. Houston: *Headache, Diagnosis and Treatment,* Philadelphia, F. A. Davis, 1959.

Garb, Solomon: *Laboratory Tests in Common Use,* ed. 2, New York, Springer, 1959.

Goldstein, Louis A.: *The Surgical Treatment of Scoliosis,* Springfield, Ill., Charles C Thomas, 1959.

Hardy, James; Griffin, J. C.; and Rodriquez, Jorge A.: *Biopsy Manual,* Philadelphia, W. B. Saunders, 1959.

Hyman, Albert Salisbury, and others: *Acute Medical Syndromes and Emergencies,* New York, Landsberger Medical Books, 1959.

Jacobovits, Immanuel: *Jewish Medical Ethics,* New York, Philosophical Library, 1959.

Long, Rowland H.: *Physician and the Law,* ed. 2, New York, Appleton-Century, 1959.

Longmore, T. A.: *Medical Photography,* ed. 5, London, Focal Press, 1955.

Moore, Francis D.: *Metabolic Care of the Surgical Patient,* Phildelphia, W. B. Saunders, 1959.

Mozes, Eugene B.: *Living Beyond Your Heart Attack,* Englewood Cliffs, N. J., Prentice-Hall, 1959.

Parsons, Willard H., and Cole, Warren H.: *Cancer of the Breast,* Springfield, Ill., Charles C Thomas, 1959.

Rider, J. Alfred, and Moeller, Hugo C.: *Disturbances in Gastrointestinal Motility,* Springfield, Ill., Charles C Thomas, 1959.

Roberts, H. J.: *Difficult Diagnosis,* Philadelphia, W. B. Saunders, 1958.

Ross Conference on Pediatric Research: *Adaption to Extrauterine Life,* report no. 31, 1959. *Disturbances of Cellular Metabolism in Infancy,* report no. 32, 1959.

Schmidt, J. E.: *Medical Discoveries Who and When,* Springfield, Ill., Charles C Thomas, 1959.

Smorodintsev, A. A.; Chudakov, V. G.; and Churilov, A. V.: *Haemorrhagic Nephroso-Nephritis,* London, Pergamon Press, 1959.

Steindler, Arthur: *Lectures on the Interpretation of Pain in Orthopedic Practice,* Springfield, Ill., Charles C Thomas, 1959.

Vegnec, Alfred J.: *Emergency Syndromes in Pediatric Practice,* New York, Landsberger Medical Books, 1959.

Vygodchikov, G. V.: *Pathogenesis and Immunology of Tumors,* London, Pergamon Press, 1959.

Wershub, Leonard Paul: *Sexual Impotence in the Male,* Springfield, Ill., Charles C Thomas, 1959.

Year Book of Obstetrics and Gynecology, 1959-60, Chicago, Year Book Publishers, 1959.

Youmans, W. B.: *Fundamentals of Human Physiology,* Chicago, Year Book Publishers, 1957.

Book Notes

Spinal Cord Compression

I. M. TARLOV, M.D., Professor of Neurology and Neurosurgery, New York Medical College, New York. 147 pages. $7.50. Springfield, Ill., Charles C Thomas Publisher, 1957.

This book, written by a neurosurgeon with much experience in experimental work, is divided into three main sections, all dealing directly or indirectly with spinal cord and cauda equina compression.

The first section is concerned with a study made on dogs in which compression of the spinal cord and cauda equina is produced by inserting a balloon into the extradural space. The study goes on to describe the effects of the compression and the changes correlated with histopathology of the spinal cord. The second section deals with spinal paralysis in man caused by trauma and/or tumor, giving symptoms, therapy, and the prognosis. The third section is devoted to the management of patients who have acute transverse lesions of the spinal cord as a result of trauma.

The author draws a conclusion to the effect that compression of spinal vessels does not play an important and significant role in the pathogenesis of acute transverse lesions of the spinal cord which may develop in patients with tumors. He concludes that a cord injury always results from the compression of the cord substances and ignores the fact that patients with metastatic carcinoma or lymphomatous tumors of the spine may develop acute transverse myelitis without any evidence of compression of the cord as determined by myelography, operation, or necropsy.

This book will be of particular interest to neurologists and neurosurgeons. The general surgeon, who may be responsible for the care of such patients, will gain much information from the section devoted to the management of acute traumatic lesions of the spinal cord.

Principles of Ophthalmoscopy

JOHN K. ERBAUGH, M.D., Norristown State Hospital, Norristown, Pa. 69 pages. $5.50. Springfield, Ill., Charles C Thomas Publisher, 1958.

This concise book is an excellent monograph on the intelligent use of the ophthalmoscope in examination of the ocular media. The basic elementary principles of examining the disk, its margins, its color, and the recognition of physiological depression are well presented for the uninitiated such as myself. The recognition of partial atrophy and of atrophy due to glaucoma and after papillitis are all well presented and discussed.

Of considerable interest to me were the sections on retinopathies due to hypertension, veinous occlusion, and anemia. Those in which organic vascular disease was a factor, such as choroidal sclerosis, macular degeneration, and diabetic lesions, were all not only well discussed, but also well illustrated with appropriate diagrams of excellent quality and beautiful color photographs of fundal changes in the various pathological lesions presented. Those who are not too skilled in the use of the ophthalmoscope are advised to read carefully the appendix to learn the method of handling the ophthalmoscope in doing a careful and systematic examination of the eye grounds and intervening media. One cannot help but improve his technique of examination if these basic principles are adhered to.

This little booklet is a valuable addition for all of those of us who use the ophthalmoscope, but who have not had any formal training in its use. It can be covered readily in an evening, and one has no hesitancy in recommending it.

—Joe C. Rude, M.D., Austin.

Neurological Basis of Behavior

G. E. W. WOLSTENHOLME and CECILIA M. O'CONNOR. 400 pages. $9. Boston, Little, Brown and Company, 1958.

This symposium on the interrelations of neural and behavioral mechanisms was arranged to mark the centenary of the birth of Sherrington. Professor G. W. Harris organized the symposium and took the chair. The United States was represented by nine of its prominent scholars. The material discussed ranged from microphysiology of neuroses to phenomena of behavior and psychology. The discussions are faithfully reported and passed on to a wider audience in this book.

Diagnostic Laboratory Hematology

GEORGE E. CARTWRIGHT, M.D., Professor of Medicine, College of Medicine, University of Utah, Salt Lake City. ed. 2. 250 pages. $6.75. New York and London, Grune and Stratton, 1958.

ORGANIZATION SECTION

★ Texas Medical Association

TMA Conference January 16 To Feature 5 Guests

Five prominent guest speakers will spark the annual Texas Medical Association's Conference of County Medical Society Officials, January 16, at the headquarters building in Austin.

Although the program is aimed toward county medical society presidents, secretaries, executive secretaries, delegates, and legislative chairmen, all members of the Association are invited to attend the one-day conference.

New and transfer members of the Association will have an opportunity to attend an Orientation Program, which will be held in conjunction with the conference, and most Association councils and committees will meet also during the week end in Austin. The meeting of the Association's Executive Board will be held January 17.

All Association members and their wives are invited to be the guests of the Association at a luncheon January 16 and at a hospitality hour that evening at the Driskill Hotel.

Physicians also are invited to attend a scientific symposium sponsored January 15 by Travis County Medical Society and Lederle Laboratories (see story in county society section).

County Officials' Conference

The President of the Texas Medical Association, Dr. F. W. Yeager, Corpus Christi, will present the keynote address at the beginning of the county officials' conference at 10:15 a.m. He will speak on "1960—A Year of Great Responsibility." The program follows:

Morning Program: 10:35 a.m.

The Stairs of Your Concepts. Dr. Marvin Vance, Austin, is in his eleventh year as pastor of the First Methodist Church of Austin. In addition to his many responsibilities of his membership of more than 3,000, he does a great deal of speaking at the annual meetings of professional, business, and trade organizations. The Austin minister is a board member for a number of civic organizations, and recently was appointed by Governor Price Daniel to the Texas Board of Corrections, which directs the work of the entire Texas Prison System.

Tax Considerations, the American Thrift Assembly, and the Physician. Dr. F. Joseph Donohue, Washington, D. C., is chairman of the board of directors of the American Thrift Assembly.

Today and Tomorrow. Allan B. Kline, Western Springs, Ill., is past president, American Farm Bureau Federation and 1958 recipient, United States Chamber of Commerce Great Living Americans Award. He has served also as president of the Iowa Farm Bureau Federation and the International Federation of Agricultural Producers. He has been abroad many times representing the Farm Bureau and the United States government.

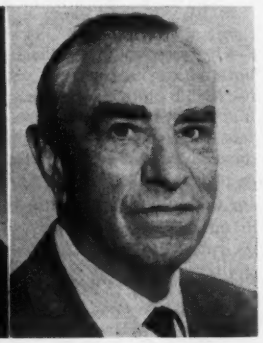
Afternoon Session: 2 p.m.

Let's Return Politics to the People. John McKee, Dallas, is regional civic and governmental affairs manager for Ford Motor Company. He has been president of the Texas Scottish Rite Hospital for Crippled Children, state chairman for the Texas Public Schools Week, president of the Dallas Crime Commission, director of the Texas Bureau for Economic Understanding, and chairman of the Dallas County, United Cerebral Palsy Association.

Panel: Achieving Greater Understanding of Health Care Costs. Dr. Russell L. Deter, El Paso, who will moderate the panel, is chairman of the Texas Medical Association's Committee on Voluntary Health Insurance. Panelists will include Dr. Arthur Kemp of Chicago, director of the Department of Medical Economics Research, American Medical Association; G. Frederick Roll of Philadelphia, director of public relations, Smith Kline and French Laboratories; and W. P. Earngey, Jr. of Fort Worth, immediate past president of the Texas Hospital Association.

The Eighty-Sixth Congress and the Forand Bill. Representative Bruce Alger of Dallas is a member of the United States House of Representatives. He has served in the House since 1954, being the first Republican to represent Dallas County. He served first as a member of the Committee on Public Works, and in 1956 was named to the Interstate and

W. P. Earngey, Jr.



Allan B. Kline

John McKee

Dr. Marvin Vance

Foreign Commerce Committee. In 1959, he was elevated to the Ways and Means Committee, centering his efforts around the Hoover Commission recommendations, fiscal responsibility, and efforts to trim the size and scope of federal government.

Orientation Program

The ninth Orientation Program for new and transfer members of the Association will be held January 16. Presiding will be Dr. James D. Murphy, Dallas, Vice-Speaker, House of Delegates, and Dr. Barton E. Park, Dallas, Vice-President, Texas Medical Association.

Morning Session: 9 a.m.

Welcome: Objectives of Orientation Program. Dr. Travis Smith, Abilene, Vice-Chairman, Board of Councilors.

The Texas Medical Association; An Accounting of Stewardship; What Happens to Your Dues? Dr. Troy A. Shafer, Harlingen, member, Board of Trustees.

Public Relations and Socio-Economic Considerations in the Practice of Medicine. C. Lincoln Williston, Austin, Executive Secretary, Texas Medical Association.

1960—A Year of Great Responsibility. Dr. F. W. Yeager, Corpus Christi, President, Texas Medical Association.

The Stairs of Your Concepts. Dr. Marvin Vance, Austin, Pastor, First Methodist Church.

Tax Considerations, the American Thrift Assembly, and the Physician. F. Joseph Donohue, Washington, D. C., Chairman, Board of Directors, American Thrift Assembly.

Today and Tomorrow. Allan B. Kline, Western Springs, Ill., Past President, American Farm Bureau Federation and 1958 Recipient, United States Chamber of Commerce Great Living Americans Award.

Afternoon Session: 1:15 p.m.

Medical Ethics Considerations in the Practice of Medicine. Dr. C. E. Oswalt, Jr., Fort Stockton, Chairman, Board of Councilors, Texas Medical Association.

Medical Etiquette; Obligations of the Physician to Colleagues and to the Profession. Dr. R. Mayo Tenery, Waxahachie, Councilor, District 14, Texas Medical Association.

Let's Return Politics to the People. Dr. John McKee of Dallas, Regional Civic and Governmental Affairs Manager, Ford Motor Company.

Serving the Doctors of Texas. Donald M. Anderson, Austin, Assistant Executive Secretary, Texas Medical Association.

Workmen's Compensation Laws; Charges, Obligations and the Law. Smith Pettigrew, Dallas, Medical Coordinator, Texas Employers' Insurance Association.

Legal Aspects of Medical Practice; Malpractice—How to Avoid It. Philip R. Overton, Austin, General Counsel, Texas Medical Association.

The Eighty-Sixth Congress and the Forand Bill. Representative Bruce Alger, Dallas, United States House of Representatives.

Hotel Accommodations

The hotels and motels named hereafter have set aside rooms for the members of the Texas Medical Association on January 15-17. Doctors are asked to make their requests directly to the facility of their choice and indicate on the request that they are members of the Texas Medical Association. Hotels: Stephen F. Austin Hotel, 701 Congress; Commodore Perry Hotel, 800 Brazos; and Driskill Hotel, 117 East Seventh. Motels: Holiday Inn Motor Hotel, 6901 Interregional Highway; Mount Vernon Motor Courts, 4001 East Avenue; Ramada Inn Roadside Motor Hotel, 5650 Interregional Highway; Terrace Motor Hotel, 1201 South Congress; and Villa Capri Motor Hotel, 2360 Interregional Highway.

26 Guest Speakers Fill Slate For TMA's Annual Session

Doctors can get their cowboy hats and boots ready for the annual session of the Texas Medical Association to be in Fort Worth next year, April 9-12.

A full slate of 26 guest speakers has accepted invitations to participate on the program. They will include Dr. William H. Bickel, Rochester, Minn., orthopedics; Dr. Benjamin Boshes, Chicago, neurology and psychiatry; Dr. Alson E. Braley, Iowa City, ophthalmology; Dr. James Barrett Brown, St. Louis, surgery; Dr. George E. Burch, New Orleans, internal medicine (heart); Dr. O. T. Clageett, Rochester, Minn., surgery; Dr. William Dameshek, Boston, internal medicine; Dr. L. Henry Garland, San Francisco, radiology; Dr. Sydney S. Gellis, Boston, pediatrics; Dr. Joseph A. Hardy, St. Louis, obstetrics and gynecology; Dr. Edward O'Neil Harper, Cleveland, Ohio, neurology and psychiatry; Dr. John R. Heller, Bethesda, Md., public health (cancer); Dr. Peter C. Kronfeld, Chicago, ophthalmology; Dr. Gordon McHardy, New Orleans, gastroenterology; Dr. Russell Meyers, Iowa City, neurosurgery; Dr. Don H. O'Donoghue, Oklahoma City, orthopedics; Dr. Louis M. Orr, Orlando, Fla., President, American Medical Association.

Among the other speakers are Dr. Ben M. Peckham, Madison, Wis., obstetrics and gynecology; Dr. Eugene P. Pendergrass, Philadelphia, radiology (cancer); Dr. John D. Porterfield, Washington, D. C., public health; Dr. Mark M. Ravitch, Baltimore, Md., surgery (cancer); Dr. James W. Reagan, Cleveland, Ohio, pathology; Dr. John J. Shea, Memphis, otolaryngology; Dr. Leroy D. Vandam, Boston, anesthesiology; Dr. J. Walter Wilson, Los Angeles, dermatology; and Dr. Walter P. Work, San Francisco, otolaryngology.

★ County Societies

Travis County Invites All To Attend Scientific Symposium

All Texas physicians are invited to attend the Travis County Medical Society's 1960 Clinical Medicine and Surgery Symposium in Austin, January 15, the day preceding the Conference of County Medical Society Officials of the Texas Medical Association. Co-sponsor is the Lederle Laboratories Division of the American Cyanamid Corporation.

Dr. George E. Clark, Jr. of Austin will moderate the morning session, and Dr. Kermit Fox of Austin will moderate the afternoon session. Dr. George W. Tipton, president of the society, will be chairman of the symposium.

Featured on the program will be Col. John P. Stapp, United States Air Force, who will talk on "Problems of Manned Space Flight"; Dr. James B. Donaldson, Laurel, Miss., "The Significance and Accuracy of Laboratory Re-

ports"; Dr. Edmund L. Dubois, Beverly Hills, Calif., "Diagnosis and Treatment of Gynecologic Diseases in the Adolescent"; Dr. Henry F. Page, Philadelphia, "What Medical Science Is Doing About Aging and the Aged"; Dr. William H. Requarth, Decatur, Ill., "The Care of Minor Farm, Home, and Industrial Injuries"; and Dr. Howard H. Steel, Philadelphia, "The Prevention and Treatment of Postoperative Infections."

All physicians of the Texas Medical Association are invited to attend the meeting and luncheon for members and their wives free of charge. A program is being planned for physicians' wives during the day. A reception will be held after the afternoon program. Doctors who desire to attend the meeting are asked to notify Roy J. Cates, Executive Secretary, Travis County Medical Society, 2907-A Red River, Austin, in advance so that necessary accommodations can be made.

County Society Briefs

Representative Frank Ikard of the Thirteenth Congressional District of Texas was honored November 11 by the *Wichita County Medical Society* with an award for outstanding public service in Congress, presented by Dr. R. L. Daily on behalf of the medical society.

Representative Frank Ikard (left) accepts an award given by the Wichita County Medical Society for outstanding public service in Congress presented by Dr. R. L. Daily (right), president of the society.

In Mr. Ikard's address to the society, he took a stand on government subsidy of medical treatment. He told the physicians that he would continue to resist the pressure and movement to enact legislation for federal subsidy of medical care.

"I don't think our committee will report favorably on the Forand bill," he told the group, adding that he would use his power to see that the bill is not adopted. "If it were adopted, complete government subsidy would not be far behind," he said.

The *Hill County Society* met November in Hillsboro. A film program on "Treatment on Chest Disease" was furnished by the Upjohn Company.

Dr. F. J. L. Blasingame, executive vice-president of the American Medical Association and past president of the Texas Medical Association, was the guest speaker at the December 7 meeting of the *Travis County Society* in Austin. Speaking off the cuff, he gave a roundup of significant items affecting medicine on the national scene. In addition to members and their wives, also in attendance were members of the Austin District Dental Society, the Seventh District of the Texas Medical Association, and the Texas Medical Association staff.

The *Harris County Society* met October 14 at the Jesse Jones Library Building in Houston. Doctors heard a panel discussion on athletic injuries, followed by a business meeting.

★ District Societies

District 12 Meet to Include M. D. Anderson Speakers

District 12 of the Texas Medical Association has planned a meeting for January 12 at the Falls Hotel in Marlin.

Speakers from the M. D. Anderson Hospital and Tumor Institute in Houston will be Dr. Clifton Howe, chief, Department of Medicine; Dr. Gerald Dodd, chief, Diagnostic Radiology; Dr. Lowell Miller, associate radiotherapist; and Dr. Nylene E. Eckles, associate internist, Medical Breast Section.

The program will cover the following topics: modern use of alkylating agents, adrenalectomy and hypophysectomy for breast cancer, place of supervoltage and its use and misuse, and radiological aid in diagnosing upper gastrointestinal tract cancer. Dr. F. W. Yeager, Corpus Christi, President, Texas Medical Association, will speak at the luncheon. Drs. Howard O. Smith, Marlin, past president, and Dr. Charles P. Hardwicke, Austin, speaker of the House of Delegates, also will participate on the luncheon program.

All members of the Texas Medical Association are welcome. Registration will begin at 9:30 a.m. For further information, those interested in attending may write Dr. J. M. Brown, Secretary, Twelfth District Medical Society, Torbett Clinic and Hospital, Marlin.

McCall Heads District 10 Society

At the annual Symposium of Current Problems in Surgery and Medicine held in Beaumont, September 19, new officers were elected for the Fifth District Chapter of Texas of the American College of Surgeons and the Tenth District Medical Society of Texas.

New officers for the Tenth District Medical Society include the following: Dr. J. W. McCall, Jr., Beaumont, president; Dr. Wallace Poshataske, Silsbee, vice-president; and Dr. Irving Richman, Beaumont, secretary-treasurer.

The Fifth District Chapter of Texas, American College of Surgeons elected the following officers: Dr. Norman Duren, Beaumont, president; Dr. John Overstreet, Houston, vice-president; and Dr. Richard Sanders, Houston, secretary-treasurer. Dr. John A. Hart, Beaumont, past president, was elected to the council.

DR. THOMAS S. MYRICK

Dr. Thomas Southall Myrick of Muenster died October 28, 1959, of a heart attack.

Born November 4, 1903, in Austin, Dr. Myrick was the son of John Southall and Anne (Brown) Myrick. He received his preliminary education in Austin and was graduated from the University of Texas in Austin in 1924 and the University of Texas Medical Branch in Galveston in 1932. He interned at Cleveland City Hospital in Cleveland, Ohio. He began practice in 1933, in Muenster, where he continued until his death.

Among the professional and civic activities in which Dr. Myrick participated were the Cooke County Medical Society, serving terms as secretary and as president; Texas Medical Association; American Medical Association; American Academy of General Practice; and County Tuberculosis Association, serving 6 years as president. He also had been director of the Muenster State Bank since 1942, president of the school board from 1953 until this year when he resigned to serve on the school district's equalization board, and president of the Lions Club for 2 years. He had served on the City Council and was city health officer.

Dr. Myrick introduced a program of immunization which is considered of great value to the community. Since he started inoculations estimated as well over 10,000 in all, Muenster has had no communicable disease.

Survivors include Dr. Myrick's wife, the former Miss Alvarene Bradshaw of Weatherford, whom he married March 30, 1932, in Lake Charles, La.; two sons, John Myrick of Houston and James Myrick of Commerce; two daughters, Mrs. Pat Stelzer of Commerce, and Mrs. Arthur Bordeau of Denton; two sisters, Mrs. Royall Watkins, Dallas, and Mrs. Marcus Fisher, Houston; and four grandchildren.

DR. THOMAS S. MYRICK

DR. D. LEON SANDERS

Dr. Dwelly Leonidas Sanders, Wills Point retired physician, died October 8, 1959.

The pioneer physician who had practiced medicine for over 60 years was a native of Ben Wheeler. He was born October 2, 1871, the son of Levi Lindsey and Suzanne (Collius) Sanders. Dr. Sanders was educated at the Alamo Institute in Ben Wheeler, receiving his premedical training at Transylvania University in Lexington, Ky. Following

DR. D. LEON SANDERS

his graduation from the Kentucky School of Medicine at Louisville, he returned to Ben Wheeler, where he began his practice of medicine. From there, he went to Edom, then Denson Springs and Eastland before settling at Wills Point. He remained at Wills Point until his death, retiring from medical practice in February, 1955.

A veteran of World War I, Dr. Sanders served 2 years in the Army Medical Corps. He was appointed regimental surgeon of the National Guard division at Wills Point and commissioned major in the Medical Corps, a post which he held for 14 years. Upon his retirement, he had the rank of lieutenant colonel.

The natural history and microscopy enthusiast was involved in a variety of civic activities in earlier years. He was a member of the Royal Arch Masons, the Blue Lodge, the Hella Temple, and the Methodist Church.

A member of the Van Zandt County Medical Society since 1906, he also belonged to the Texas Medical Association and was elected to honorary membership in this organization in 1950. Other medical memberships which he held included the American Medical Association, and formerly the Southern Medical Association.

Members of the family surviving Dr. Sanders include his wife, the former Miss Nell Wren Williams of Marshall; three daughters, Mrs. Constance Sanders Todd of Independence, Kan., Miss Blanche Sanders of New York, and Miss Mary Lee Sanders of Dallas; two stepsons; a stepdaughter; four grandchildren; and a sister, Mrs. J. H. Cates of Seagoville.

DR. ANDREW S. TOMB

Dr. Andrew Spencer Tomb of Victoria, former president of the Texas Academy of General Practice and former vice-president of the Texas Medical Association, died in Louisiana August 26, 1959, after having a heart attack, his third in recent years.

In demand as a speaker before both medical and non-medical audiences, Dr. Tomb was born at Jackson, La., September 12, 1910. He received his premedical training at Louisiana State University at Baton Rouge and was graduated in 1933 from Tulane University School of Medicine at New Orleans, followed by an internship at the New Orleans Charity Hospital. Staying in Louisiana, Dr. Tomb practiced at Jackson, Baton Rouge, and Shreveport. He

DR. ANDREW S. TOMB

then moved to Texas, practicing at Kilgore and Seminole, before going to Victoria. He remained there until August, when he closed the Victoria Medical and Surgical Clinic which he had operated for several years. He was in the process of returning to his native Louisiana when he died.

Although a general practitioner, the field of psychiatry greatly interested Dr. Tomb. Immediately preceding his death, he had made arrangements to join a psychiatric research development at Tulane University School of Medicine. He also was instrumental in the movement for better liaison between the American Psychiatric Association and the American Academy of General Practice. His interest in mental illness brought about his appointment by Governor Allan Shivers in 1953 to a 4 year term on the Texas Commission on Alcoholism.

Active in a variety of medical organizations, Dr. Tomb was a member of the House of Delegates of the Texas Medical Association and of its Committee on Alcoholism. He was a past president of the Eighth District Medical Society, a past secretary for the Dawson-Lynn-Terry-Gaines-Yoakum Counties Medical Society and a past secretary and president of the Victoria-Calhoun-Goliad Counties Medical Society. He was a member of the American Academy of General Practice, belonged to this organization's congress of delegates and was a member of several of its committees. Dr. Tomb was a member of the Committee on Mental Health for the American Medical Association, served on several committees of the Texas Academy of General Practice, was a mental health consultant for the Texas State Department of Health, and was on the editorial advisory boards of the *Heart Bulletin, Cancer Bulletin, Current Medical Digest,* and *Medical Economics.* A pilot, Dr. Tomb sometimes used a plane in his medical practice.

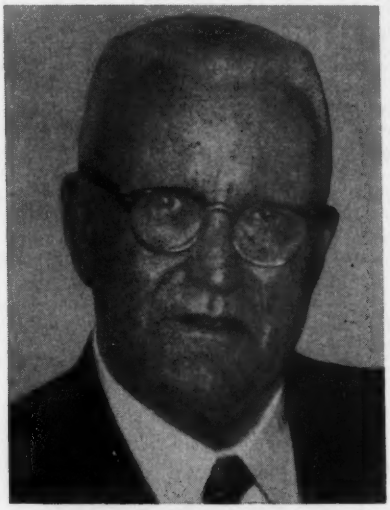
Dr. Tomb was president of the board of trustees for the Victoria Independent School District for 3 years and was a consultant for the Southern Regional Education Board.

Members of the family who survive include his wife; his son, Spencer Tomb of Victoria; two daughters, Miss Helen Grace Tomb and Miss Sarah Tomb, both of Minden; a stepson, Gary Schaffstall of Victoria; his mother, Mrs. Helen Tomb of Minden; and two sisters, Miss Grace Tomb of Jackson and Miss Helen Tomb of New Iberia, La.

DR. CHRISTIAN M. COTHAM

Dr. Christian Malford Cotham, San Antonio general practitioner, died October 3, 1959, of a mild cardio infarction and severe arteriosclerotic heart disease.

Dr. Cotham was born in Bonham, January 17, 1888, the son of James Clark and Narcissus (Cox) Cotham. He attended schools in Bertram and in 1909 was graduated from the University of Texas Medical Branch at Galveston. He did postgraduate work in Mayo Clinic and other clinics



DR. CHRISTIAN M. COTHAM

throughout the country. His practice in San Antonio began in 1920; prior to that he had practiced at Burnet and at Scherts. He was a staff member of Baptist Memorial, Santa Rosa, and Nix Hospitals.

The physician had been a member of the Texas Medical Association since 1911, his latest membership in this organization through the Bexar County Medical Society. In the past, he had belonged to the Burnet County Medical Society as well as the Guadalupe County Medical Society. He also held membership in the American Medical Association, Southern Medical Association, and was an associate of the International College of Surgeons. His affili-

ations with civic and religious groups included the First Presbyterian Church, the Masonic Lodge, Scottish Rite bodies, Alzafar Shrine, Woodmen of the World, Pretorians, Elks, and Herman Sons.

Dr. Cotham and the former Miss Forrest Hudson of Caldwell were married at Cameron in 1912. Mrs. Cotham died in 1952.

Surviving are a son, Mayor Christian M. Cotham and two daughters, Mrs. Margaret Spence of San Antonio and Mrs. Virginia Carlson of El Campo; a sister, Miss Alma Cotham of Burnet; and five grandchildren, Parker James Spence, Jr., Christian Malford Cotham III, Jeffrey Clark Cotham, Carl J. Carlson, Jr., and Cathryn Carlson.

DR. BERTHA PATTERSON

Dr. Bertha Schenck Stecker McDavitt Patterson, who practiced in Temple for about 40 years until her retirement in 1952, died in Fort Worth October 23, 1959.

Dr. Patterson was born September 6, 1877, in Burlington, Iowa. She was a graduate of the State University of Iowa College of Medicine at Iowa City and practiced at Bonaparte, Iowa, for 3 years and Burlington, Iowa for another 3 years before moving to Temple in 1913.

She specialized in disease of the eye, ear, nose, and throat. For many years Dr. Patterson was associated with Dr. J. M. Woodson on the staff of Scott and White Hospital. Following Dr. Woodson's death, she maintained her own office in the Temple National Bank building.

DR. BERTHA PATTERSON

Elected to honorary membership in the Texas Medical Association in 1954, she had belonged to this organization since 1915. Since her move to Fort Worth, she had belonged to the Tarrant County Medical Society. Prior to that she was a member of the Bell County Medical Society. Other medical organizations to which Dr. Patterson belonged included the American Medical Association and the American Academy of Ophthalmology and Otolaryngology. She was a fellow of the American College of Surgeons, a member of the Grace Presbyterian Church while in Temple, a past president of the Temple Business and Professional Women's Club, a member of the Eastern Star, and a member of Delta Kappa Gamma and Delta Delta Delta sororities.

About 2½ years ago she married the Rev. E. R. Patterson, a Methodist minister, who survives. Also surviving are a son, Walter F. Stecker of Fort Worth; two brothers, Dr. C. P. Schenck of Fort Worth and Dr. W. L. Schenck of Iowa City, Iowa; a sister, Miss Mary E. Schenck of Boca Raton, Fla.; three grandchildren; and eight great grandchildren.

DR. WILLIAM E. BARNETT

Dr. William Edwin Barnett, Dallas, died November 2, 1959, of acute myocardial infarction.

A native of Logansport, Ind., Dr. Barnett was born February 25, 1905, the son of George E. and Roxie (Conrad) Barnett. He attended Indiana public schools and was graduated from the DePauw University at Greencastle, Ind., and cum laude from the Indiana University School of Medicine at Indianapolis. He served an internship and residency at the Indiana University Hospital, also at Indianapolis and did postgraduate work at the Harvard Medical School, the Boston City Hospital, and the Massachusetts General Hospital. In 1933 he began practicing medicine at Logansport, left his practice in 1941 to serve as a lieutenant colonel in the Army Medical Corps, and at the end of his military service in 1946, moved to Dallas. His practice there was limited to internal medicine and cardiology.

Dr. Barnett's memberships in professional organizations included the American Medical Association, the Texas Medical Association, and the Dallas County Medical Society. He also belonged to the American Heart Association and Alpha Omega Alpha honorary medical fraternity, was a diplomate of the American Board of Internal Medicine, and previously had belonged to the Cass (Indiana) County Medical Society and the Indiana State Medical Society. Dr. Barnett listed fishing and photography as his hobbies.

In 1936 Dr. Barnett married the former Miss Mary John Embree of Owensville, Ind. They have two children, Sarah and Stephen. All survive.

DR. WILLIAM E. BARNETT

DR. EMMETT CRUMPLER

Dr. Walter Emmett Crumpler, Port Arthur gynecologist, died September 28, 1959, as a result of a heart attack.

Born in Rockland January 15, 1911, Dr. Crumpler was the son of Dr. Walter Emmett and Sue Mae (Edwards) Crumpler. He attended Port Arthur schools, the University of Texas at Austin, and Tulane University School of Medicine at New Orleans. He received his degree of doctor of medicine in 1936, and after an internship at the Shreveport Charity Hospital in Shreveport, La., began his practice of gynecology in Port Arthur. During World War II, Dr. Crumpler served as a major with the United States Army.

Dr. Crumpler's memberships in medical organizations included the Jefferson County Medical Society, the Texas Medical Association, the American Medical Association, and the Southwestern Surgical Congress. He belonged to Alpha Tau Omega social fraternity, the Chamber of Commerce, the Methodist Church, and the Country Club.

The physician's survivors include his wife, the former Miss Alleen Picket of Houston (they were married in 1931); a daughter, Karin; and his mother, Mrs. Sue Crumpler, all residing in Port Arthur.

DR. ORAN H. TALLEY

Dr. Oran Hubbell Talley, Corpus Christi, died September 11, 1959, of carcinoma.

Dr. Talley was the son of J. Allen and Lydia (Brown) Talley, born December 18, 1884, in Leesville. He was graduated in 1911 from the University of Texas Medical Branch at Galveston, after which he served an internship at St. Vincent's Hospital at Sherman. The following year he married the former Miss Mary Ellen Towell of Sherman. They had no children.

Following an internship at St. Vincent's Sanitarium at Sherman, Dr. Talley opened a general practice at Van Horn. From there he moved to El Paso, then left Texas and practiced in Mexico for 17 years as a physician to the American Smelting and Refining Company. He returned to Texas in 1940, practiced at Seguin for 2 years, then moved to Corpus Christi, where he had a general practice and was a physician again for the American Smelting and Refining Company. His years of practice were interrupted by a brief period of service as first lieutenant in the Army Medical Corps during World War I.

Dr. Talley's memberships in medical organizations included the Nueces County Medical Society, the Texas Medical Association, and the American Medical Association. Previously, he had belonged to the Guadalupe County Medical Society. He was a Catholic, and was a member of the Knights of Columbus and Knights of Alhambra.

Surviving Dr. Talley are his wife, and two brothers, J. Allen Talley of San Angelo and Emory E. Talley of Port Arthur.

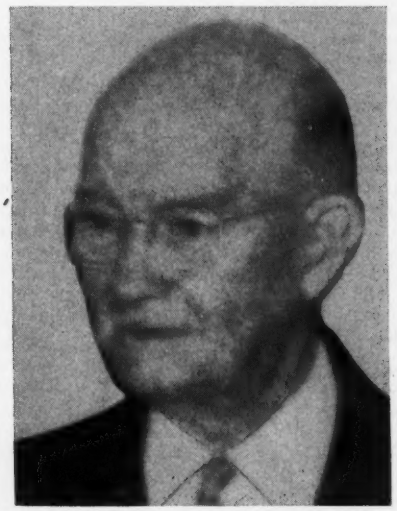
DR. M. A. CUNNINGHAM

Dr. Michael Angelo Cunningham, medical director and superintendent of the Jefferson County Tuberculosis Hospital at Beaumont, died September 20, 1959, of acute coronary thrombosis.

A specialist in chest diseases, he was a native of Malvern, Iowa, born August 24, 1889, to Michael and Margaret (Aistrope) Cunningham. He attended Malvern schools and was graduated in 1913 from Creighton Medical College at Omaha, Neb., followed by an internship at St. Mary-Corwin Hospital in Pueblo, Colo.

Following the death of his sister, Mrs. Lillian Neas, from tuberculosis in 1915, he became deeply concerned with the problem of this disease, and the remaining 44 years of his life were spent in anti-tuberculosis work, first as assistant superintendent of the Iowa State Sanatorium at Oakdale, then as medical director of Holy Cross Sanatorium in Deming, N. Mex. In 1939 he accepted the superintendency of Jefferson County Tuberculosis Hospital in Beaumont, where he served until his death.

Dr. Cunningham was one of the 39 men who met at Albuquerque, N. Mex., in 1935 to form an organization for the purpose of educating the general practitioner in early diagnosis of tuberculosis. From this nucleus of 39 men developed what is today the American College of Chest Physicians. He was a member of the Jefferson County Medical Society, the Texas Medical Association, the Amer-



DR. ORAN H. TALLEY

DR. M. A. CUNNINGHAM

ican Medical Association, and the Southwestern Medical Association. He also belonged to the National Tuberculosis Association and the American Trudeau Society. He served for 15 years as a director of the Texas Tuberculosis Association and as medical director for both the Beaumont and the Port Arthur Tuberculosis Associations. Previously, he had been a member of the New Mexico State Medical Society and the Luna County (New Mexico) Medical Society. Dr. Cunningham belonged to the Royal Arch of the Masonic Order.

Members of the family who survive include his wife, the former Miss Harriett M. Miller of Waterloo, Iowa; a son, Robert E. Cunningham of Huntsville, Ala.; a brother, Donald O. Cunningham of Los Angeles; and two sisters, Mrs. Bernard Hume of Olympia, Wash., and Mrs. Frederick Buttmann of Malvern, Iowa.

DR. JOSEPH H. ALLEN

Dr. Joseph H. Allen, Justin, former president of the Denton County Medical Society, died September 28, 1959.

The 82 year old physician was a native of Sycamore, the son of Dr. and Mrs. T. B. Allen. He was a graduate of the old Fort Worth Medical College and had done postgraduate work at the Chicago Polyclinic, Tulane University School of Medicine at New Orleans, and at Baylor University College of Medicine at Houston.

Dr. Allen had lived in Denton since his retirement in 1956. Prior to that he had practiced medicine 55 years in Justin and the surrounding communities of Ponder, Krum, Argyle, Keller, Bartonville, Watauga, Rhome, Newark, Boyd, and Haslet.

A member of the Texas Medical Association since 1904, Dr. Allen was elected to honorary membership in this group in 1955. He was instrumental in organizing the Denton County Medical Society and was its president in 1941. Active also in community affairs, he helped organize the Justin State Bank, of which he had served as president and as a director for many years.

Survivors are his wife, the former Miss Effie McDaniel, whom he married at Sycamore in 1907; two sons, J. E. Allen and C. E. Allen of Denton; a daughter, Mrs. J. E. Jones of Pauls Valley, Okla.; a sister, Mrs. Tressie Johnson of Alvord; and 11 grandchildren.

DR. THOMAS L. GOODMAN

Dr. Thomas L. Goodman, past president of the Tarrant County Medical Society, died August 4, 1959.

The Fort Worth physician was a native of Springtown (he was born in 1882 to Zibulon Pike and Mary Ann Goodman) and taught school in Parker County before attending the Medical Department of Texas Christian University at Fort Worth. He served an internship at the Medical College Hospital in Fort Worth, and at various times he was pathologist for Harris Sanitarium, St. Joseph's Infirmary, the Fort Worth and Denver Railroad, and the Gulf Colorado and Santa Fe Railroad. He also had been professor of pathology at the Medical Department of Texas Christian University. He did postgraduate work at the Chicago Eye, Ear, Nose, and Throat Hospital and School, the New Orleans Eye, Ear, Nose, and Throat Hospital, and the Colorado Eye, Ear, Nose, and Throat Assembly. He served on the staff of City-County Hospital (now Peter Smith Hospital) in Fort Worth for some 25 years. Fellow staff members presented him with a plaque for his charity work at the hospital. He was a pharmacist in Clarendon before going in 1909 to study medicine in Fort Worth, where he practiced until 7 years before his death. He had retired from medical practice because of illness.

Dr. Goodman and Miss Arrie Neill of Springtown were married in 1904. Mrs. Goodman died in 1956.

Dr. Goodman's professional memberships included the Texas Medical Association, an organization to which he had been elected to honorary membership in 1953; the American Medical Association; the American Academy of Ophthalmology and Otolaryngology; District 13 Medical Society; and the Fort Worth Eye, Ear, Nose, and Throat Society. He was a member of Fort Worth Masonic Lodge No. 148, the Royal Arch Masonic Lodge No. 362, and the Christian Church.

Surviving are a daughter, Mrs. Clifton H. Lawrence of Fort Worth, and three grandchildren.

DR. CHARLES H. McCOLLUM, JR.

Dr. Charles Holmes McCollum, Jr., Fort Worth physician since 1935, died October 5, 1959, after having a heart attack.

The general surgeon was born at Hico but attended public schools in Fort Worth. He was the son of Dr. Charles H. and Nancy Eunice (Holmes) McCollum. He also attended Texas Christian University and the University of Texas, and in 1933 was graduated from Tulane University Medical School in New Orleans. After an internship and residency at John Peter Smith Hospital in Fort Worth, he started his medical practice in that city. His practice was limited to general surgery and internal medicine. He was chief of the gynecology service at John Peter Smith Hospital and a member of the executive committee and past chief of staff at St. Joseph's Hospital, also in Fort Worth.

During the late 1930's and early 1940's, Dr. McCollum held a number of civic offices, including state and local directorships of the Junior Chamber of Commerce. He was also local president and national councilor of the Fort Worth Junior Chamber of Commerce and was given the United States Junior Chamber of Commerce Distinguished Service Award in 1940. That same year he was named Fort Worth's outstanding young man of the year. During World

DR. CHARLES H. McCOLLUM, JR.

War II he was a lieutenant commander in the United States Navy, serving as a surgeon in hospitals in San Diego, Calif., and in the Pacific. Dr. McCollum was a member of the board of commissioners of the Fort Worth Housing Authority, a member of the University Christian Church, Fort Worth Rotary Club, the Colonial Country Club of Fort Worth, and the Steeplechase Club of Fort Worth. He also had served as a member of the board of directors of the Children's Museum.

Dr. McCollum's medical affiliations included membership in the Tarrant County Medical Society, the Texas Medical Association, the Fort Worth Academy of Medicine, and the American Medical Association.

In 1930 Dr. McCollum and the former Miss Mary Gladys Beck of Fort Worth were married. She survives as do two sons, Dr. Charles H. McCollum, III, who is interning at the University of Pennsylvania Hospital, and Richard G. McCollum, a student at the University of Pennsylvania Medical School; a daughter, Miss Gayle McCollum of Fort Worth; and a sister, Mrs. Ray Reeder of Denton.

DR. JOHN W. GOODE, SR.

Dr. John William Goode, Sr., San Antonio, died August 30, 1959, of a coronary occlusion.

A resident of San Antonio for 50 years, Dr. Goode was born in Holland, Texas. The 73 year old physician received his preliminary education at Hardin-Simmons University, Abilene, and at the University of Texas Medical Branch at Galveston. He served an internship at Santa Rosa Hospital in San Antonio. He was medical director of the Alamo Life Insurance Company and was former chief of staff at the Medical and Surgical Hospital of San Antonio. He was in the United States Army Medical Corps during World War I, holding the rank of first lieutenant. Dr. Goode began his practice in San Antonio in 1913 and conitnued it until his death. Formerly, he had been chairman of the San Antonio Board of Health, chief surgeon of the Missouri Pacific Railroad, and the Missouri-Kansas-Texas Railroad.

Dr. Goode was a past president of the Bexar County Medical Society and was a member of the Texas Medical Association, the American Medical Association, the Texas Surgical Society, the International Medical Assembly of Southwest Texas, American Association of Railway Surgeons, and the Texas Traumatic Surgical Society.

He was a fellow of the American College of Surgeons. Dr. Goode was a member of the Veterans of Foreign Wars; he also was a Mason.

The physician is survived by his wife, the former Miss Claudia Nolte of Seguin whom he married in 1916; one son, John William Goode, Jr.; two daughters, Miss Claudia Goode and Mrs. David Brune, all of San Antonio; a brother, R. Jones Goode of Plainview; and six sisters, Mrs. Ellis Carter and Mrs. Harold Bawden of Plainview; Mrs. R. H. Hughes of Cedar Rapids, Iowa; Mrs. Paul Stockton of Redlands, Calif.; Mrs. Mohler Temple of Lubbock; and Mrs. E. T. McTeer of Fort Worth.

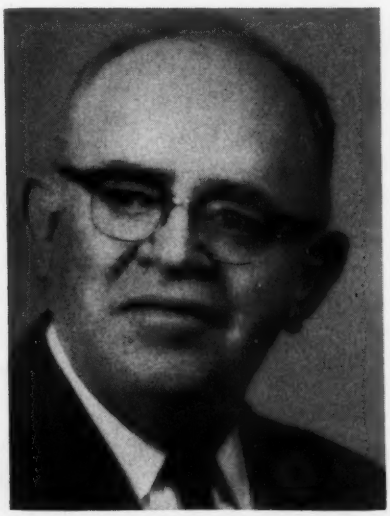
DR. JOHN PARKER EATON

Dr. John Parker Eaton, Rusk, died September 24, 1959, at his home.

The native Texan was born at Overton March 27, 1908. He attended the University of Texas at Austin and was graduated in 1941 from the Arkansas School of Medicine at Little Rock. After a year's internship at St. Vincent's Infirmary at Little Rock, he joined the United States Air Force, seeing service in Iwo Jima. He was awarded the bronze star in 1945 and was discharged with the rank of major. He started his medical practice at Rusk in 1949.

A member most recently of the Jefferson County Medical Society, Dr. Eaton previously had belonged to the Cherokee County Medical Society and the Travis County Medical Society. He belonged to the Texas Medical Association until 1953, retiring that year because of ill health. He was a Baptist.

Members of the family who survive include Dr. Eaton's wife, Mrs. Edna Eaton; two sons, John and James Eaton of San Angelo; a daughter, Mrs. Jewel Hill of Bridge City; three brothers, Virgil Eaton of Rhome, J. L. Eaton of Henderson, and Otis Eaton of Tyler; three sisters, Mrs. Hubert Crim, Mrs. Robert Poole, and Mrs. Claud Mullins, all of Henderson; and three grandchildren of Bridge City.



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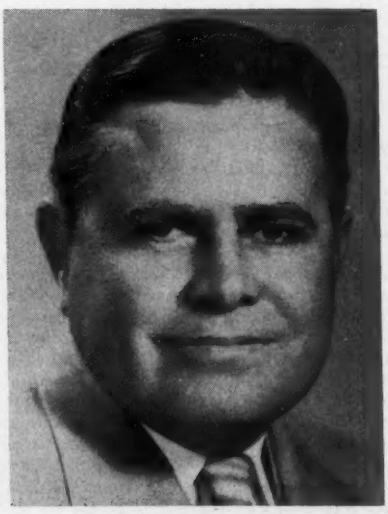

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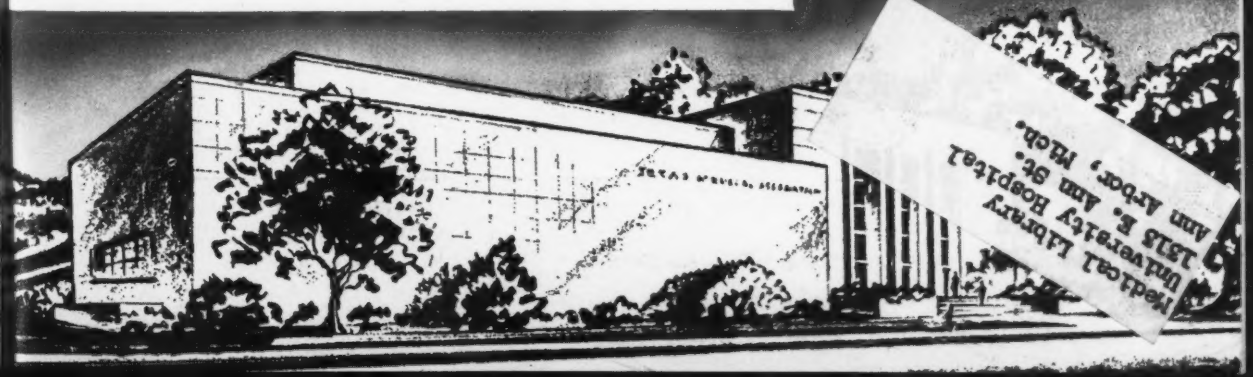

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Texas State Journal of Medicine is published monthly by the Texas Medical Association. Subscription price, $3 per year for members; $6 for nonmembers; $7 for foreign. Single copy, 75 cents.

Entered as Second Class Matter July 1, 1905, at the Post Office at Fort Worth, Texas, under act of March 3, 1879.

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CONTRIBUTIONS

Previously unpublished manuscripts are welcomed for review; suggestions for preparation are available from the Editorial Offices. News and other items should be sent to the Editorial Offices by the twentieth of the month preceding publication. All contributions are sent at the owner's risk.

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Advertising rates are available on request. Electrotypes should be shipped to the Printing Offices to arrive by the fifteenth of the month preceding publication.

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SUBSCRIPTIONS

Subscription communications should be sent to the Business Offices.
$3 per year for members
$6 for nonmembers; $7 for foreign.
Single copy: 75 cents.

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PAPER ELECTROPHORESIS, A DIAGNOSTIC AID IN GENERAL MEDICINE

It has been 20 years since Longsworth, Shedlovsky, and MacInnes published their classic work on electrophoretic patterns of normal and pathological human blood serum and plasma. Since that time, many papers expanding this basic work have appeared in clinical publications. As the technical problems in electrophoretic work have been overcome the technique has become more widely used by clinicians both as a diagnostic and prognostic aid in many pathologic conditions.

The principle of electrophoresis is based on the observations that proteins have an electric charge. When placed in an electric field, the proteins will migrate at a rate in accordance with their individual electric charge. After a known period of time the strip of paper along which they migrate is removed from the electric field and the proteins are demonstrated by combining them with dyes. By this method accurate quantitative estimations of the different proteins in the sample can be obtained.

Bruten in 1952 pointed out the association between a wide variety of recurrent infections and the failure of the body to produce gammaglobin. He called this disease entity Agammaglobulinemia. The only method to detect this congenital anomaly is through the study of the serum proteins.

Multiple myeloma is almost invariably associated with abnormalities of the electrophoretic protein pattern. In a large percentage of cases an abnormal "m" globulin can be demonstrated.

Nephrosis presents a clear cut abnormal electrophoretic pattern first described by Longsworth. The lowered albumin and greatly increased alpha-2-globulin is diagnostic of this disease entity.

The electrophoretic pattern of serum is of considerable aid in the differential diagnosis of obstructive jaundice, hepatitis and cirrhosis. In cirrhosis the albumin is low and the gammaglobulin is markedly increased. In contrast the serum protein pattern for hepatitis shows a normal albumin but also an increased gammaglobulin. In obstructive liver disease there is usually no significant protein pattern change.

Another group of diseases lends itself well to study by the electrophoretic method. These are the congenitally abnormal hemoglobins such as are associated with sickle cell disease and thalassemia. At least ten different types of abnormal hemoglobins have been described since 1949.

Spinal fluid also is amenable to assay by this method. Yahr has shown in a series of 681 patients with neurologic diseases that cerebral spinal fluid gammaglobulin is increased in 67% of those with multiple sclerosis, 75% of those with neurosyphilis, and in only 6% of those with other diseases of the nervous system.

SUMMARY

Electrophoresis is an extremely useful diagnostic and prognostic tool in many pathologic conditions, particularly hepatic and renal disorders, Agammaglobulinemia, multiple myeloma, lupus erythematosus, certain rheumatoid diseases, hemoglobin abnormalities and some diseases of the central nervous system.

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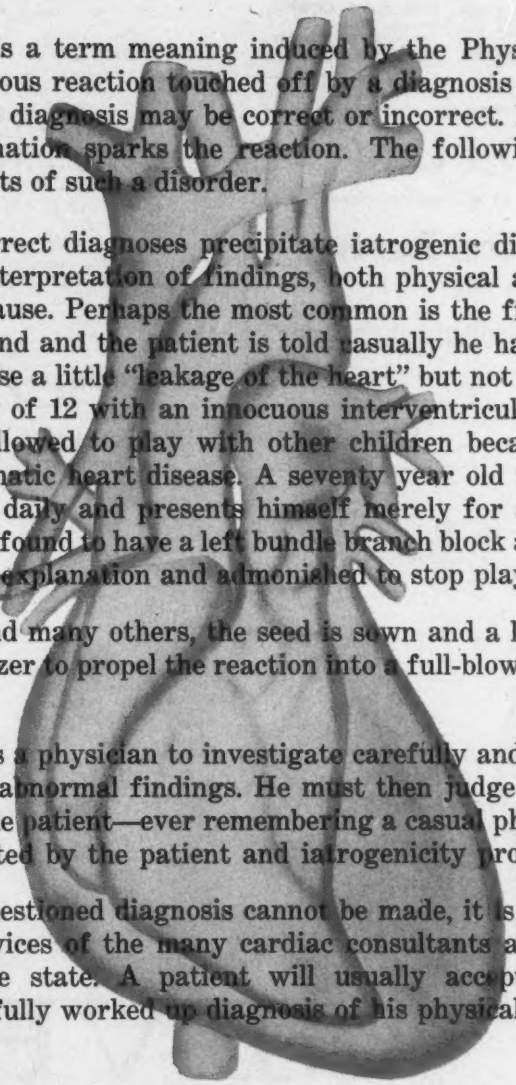

Iatrogenic is a term meaning induced by the Physician. It refers to a nervous reaction touched off by a diagnosis given to the patient. The diagnosis may be correct or incorrect. In either case, the explanation sparks the reaction. The following illustrate both aspects of such a disorder.

Many incorrect diagnoses precipitate iatrogenic disease. In the main, misinterpretation of findings, both physical and laboratory, is the cause. Perhaps the most common is the finding of a split first sound and the patient is told casually he has a little murmur or worse a little "leakage of the heart" but not to worry about it. A boy of 12 with an innocuous interventricular septal defect is not allowed to play with other children because of a supposed rheumatic heart disease. A seventy year old man who is playing golf daily and presents himself merely for a routine examination, is found to have a left bundle branch block and given a too elaborate explanation and admonished to stop playing golf.

In these and many others, the seed is sown and a little time acts as a catalyzer to propel the reaction into a full-blown cardiac neurosis.

It behooves a physician to investigate carefully and evaluate thoroughly all abnormal findings. He must then judge critically what he tells the patient—ever remembering a casual phrase may be misinterpreted by the patient and iatrogenicity produced.

If an unquestioned diagnosis cannot be made, it is advisable to use the services of the many cardiac consultants and clinics throughout the state. A patient will usually accept without anxiety a carefully worked up diagnosis of his physical status.

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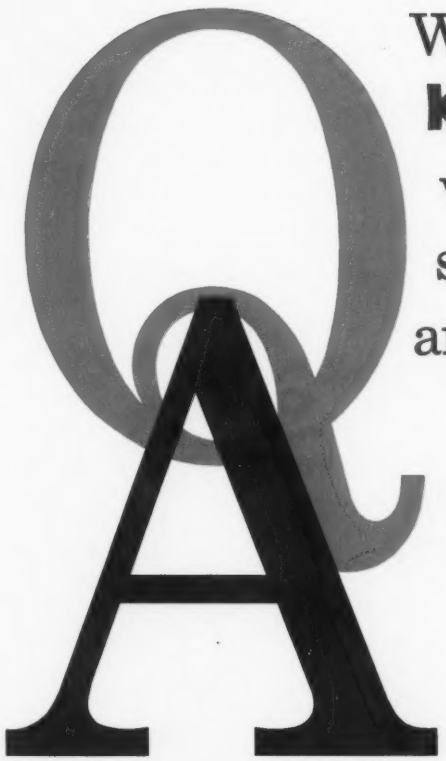

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A A very good question, but it is reassuring to note that in almost two years of clinical use of KANTREX for the treatment of infections for which it is recommended, the emergence of KANTREX-resistant bacterial populations has not been a problem.

Q *My impression is that* KANTREX *is just another neomycin. Isn't that so?*

A Indeed not. The only thing KANTREX and neomycin have in common is a similar antimicrobial spectrum. Otherwise, they're very different: they have different chemical structures; the toxicity of KANTREX is "much less than that of neomycin"[14]; and clinically, KANTREX Injection is practical for systemic administration routinely, while neomycin is not.

Q *You mean that* KANTREX *Injection doesn't have the nephrotoxicity of neomycin?*

A Precisely. It's true that when KANTREX Injection is used, urinary casts – even slight albuminuria or microscopic hematuria – may appear, especially in poorly hydrated patients, but this does not reflect any progressive damage to the kidneys. These signs promptly disappear on adequate hydration or termination of therapy.

Q *Then why do you recommend reduced dosage in patients with renal impairment?*

A Because renal impairment causes an excessive accumulation of KANTREX in the blood and tissues, when usual doses are administered. Since KANTREX Injection is excreted entirely by the kidneys, renal impairment leads

to unnecessarily high and prolonged blood levels; and such excessive concentrations increase the risk of ototoxicity.

Q *Is that why we see reports of patients developing hearing loss during* KANTREX *Injection therapy?*

A Yes. A study of the few reported cases in which patients have suffered impaired hearing will show that in every instance they had pre-existing or concurrent renal impairment, yet received usual or excessive doses of KANTREX Injection. Dosage recommendations for KANTREX Injection emphasize that in patients with renal dysfunction, adequate serum levels can be achieved with a fraction of the dose suggested for patients with normal kidney function – with minimal risk of ototoxicity.

Q *Since urinary tract infections are often accompanied by renal impairment, does that mean I shouldn't use* KANTREX *Injection in such conditions?*

A Not at all. With proper precautions, KANTREX Injection is an excellent drug for the treatment of urinary tract infections, especially those due to *Proteus*, *A. aerogenes* and *E. coli*, even when renal impairment is present.

Q *What are the "proper precautions" in a patient with impaired renal function?*

A The package literature covers them in detail. First, the daily dose should be reduced in such a patient. Then, if he is going to receive KANTREX Injection for 7 days or more, a pre-treatment audiogram should be done, and it should be repeated at appropriate intervals during therapy. If tinnitus or subjective hearing loss develops, or if followup audiograms show significant loss of high frequency response, KANTREX therapy should be discontinued. However, therapy for 7 days or more

is seldom required because the clinical response to KANTREX Injection is so rapid.

Q *Why do you put so much emphasis on* KANTREX'S *"rapid action"? Every antibiotic I've heard about is supposed to be "rapid acting."*

A There is such an abundance of clinical evidence about "rapid acting" that it takes KANTREX Injection out of the "supposed-to" class.[1,2,3,7,8,9,11,15,16,19,21,22,26,29,32,33] Remember, the effectiveness of KANTREX Injection therapy can usually be appraised in 24 to 36 hours. That's definite evidence of rapid action. In fact, one group of investigators reported that "the rapidity with which bacteria are killed by this agent is reflected by the promptness of the clinical response."[29]

Q *Does* KANTREX *Injection cause blood dyscrasias?*

A In extensive clinical and toxicity studies by numerous investigators, as well as almost two years of general use, not a single instance of such toxicity has been reported.

Q *Can I administer* KANTREX *Injection in any other way than by the intramuscular route?*

A Yes. While it's usually given intramuscularly, other routes are practicable: intravenous, intraperitoneal, by aerosol, and as an irrigating solution. Complete instructions are included in the package insert.

Q *So you think I ought to use* KANTREX *Injection as my first choice antibiotic in staph and gram-negative infections?*

A Yes – because all evidence to date indicates that it is bactericidal against a wide range of organisms...rapid acting...does not encourage development of bacterial resistance...is well tolerated in specified dosage...and has not caused any blood dyscrasias.

KANTREX® CAPSULES

for local gastrointestinal therapy... not for systemic infections

Q *Why can't I use* KANTREX *Capsules for systemic medication?*

A Because there is only negligible absorption of KANTREX from the gastrointestinal tract.[3,5,6,8,28,34] Thus, capsules cannot provide effective blood levels.

Q *Then what are* KANTREX *Capsules used for?*

A Preoperative bowel sterilization, and local treatment of intestinal infections due to kanamycin-sensitive organisms.

Q *I've been using neomycin for preoperative bowel sterilization. Why should I switch to* KANTREX *Capsules?*

A Because KANTREX has been rated as "superior to neomycin" for this purpose.[6] It provides rapid and satisfactory control of coliforms, clostridia, staphylococci and streptococci; yeasts do not proliferate; stool concentrations of the drug are exceptionally high; and nausea, vomiting or intestinal irritation have not been observed.[5,6]

Q *What advantages do* KANTREX *Capsules offer me in the treatment of intestinal infections?*

A A high degree of effectiveness against most of the pathogens responsible for such infections: *Salmonella, Shigella, Staph. aureus, E. coli* and *Endamoeba histolytica.* Moreover, their use has been "remarkably free of any side effects."[31]

KANTREX®

INJECTION KANAMYCIN SULFATE INJECTION

INDICATIONS

Infections due to kanamycin-sensitive organisms, particularly staph or "gram-negatives": genito-urinary infections; skin, soft tissue and post-surgical infections; respiratory tract infections; septicemia and bacteremia; osteomyelitis and periostitis.

DOSAGE: INTRAMUSCULAR ROUTE

Recommended daily dose is 15 mg. per kg. of body weight, in 2 to 4 divided doses.

For intramuscular administration, KANTREX Injection should be injected deeply into the upper outer quadrant of the gluteal muscle.

TOXICITY

When the recommended precautions are followed, the incidence of toxic reactions to KANTREX is low. In well hydrated patients under 45 years of age with normal kidney function, receiving a total dose of 20 Gm. or less of KANTREX, the risk of ototoxic reactions is negligible.

In patients with renal disease and impaired renal function, the daily dose of KANTREX should be reduced in proportion to the degree of impairment to avoid accumulation of the drug in serum and tissues, thus minimizing the possibility of ototoxicity. In such patients, if therapy is expected to last 7 days or more, audiograms should be obtained prior to and during treatment. KANTREX therapy should be stopped if tinnitus or subjective hearing loss develops, or if audiograms show significant loss of high frequency response.

OTHER ROUTES OF ADMINISTRATION

KANTREX should be used by intravenous infusion only when the intramuscular route is impracticable. KANTREX can also be employed for intraperitoneal use, aerosol treatment, and as an irrigating solution. See package insert for directions.

PRECAUTIONS

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection appears during therapy, appropriate measures should be taken.

SUPPLY

Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations (stable at room temperature indefinitely):

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume.
KANTREX Injection, 1.0 Gm. kanamycin (as sulfate) in 3 ml. volume.

CAPSULES (for local gastrointestinal therapy; not for systemic medication)

INDICATIONS AND DOSAGE

For preoperative bowel sterilization: 1.0 Gm. (2 capsules) every hour for 4 hours, followed by 1.0 Gm. (2 capsules) every 6 hours for 36 to 72 hours.

For intestinal infections: Adults: 3.0 to 4.0 Gm. (6 to 8 capsules) per day in divided doses for 5 to 7 days. Infants and children: 50 mg. per kg. per day in 4 to 6 divided doses for 5 to 7 days.

PRECAUTION

Preoperative use of KANTREX Capsules is contraindicated in the presence of intestinal obstruction. Although only negligible amounts of KANTREX are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be considered.

SUPPLY

KANTREX Capsules, 0.5 Gm. kanamycin (as sulfate), bottles of 20 and 100.

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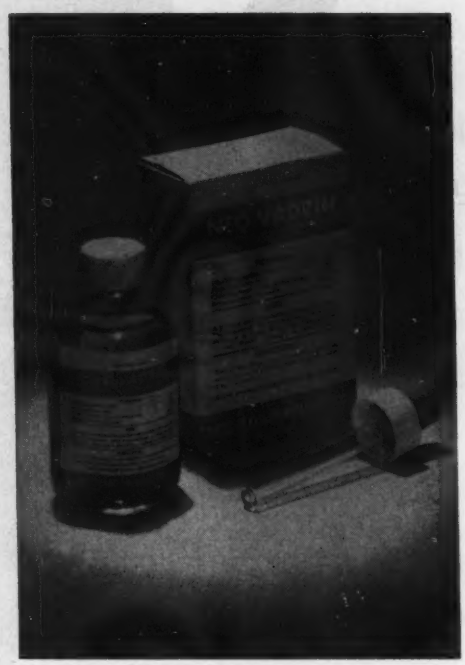

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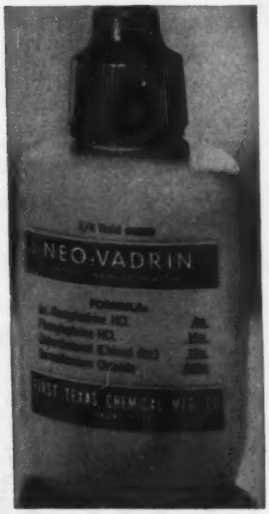

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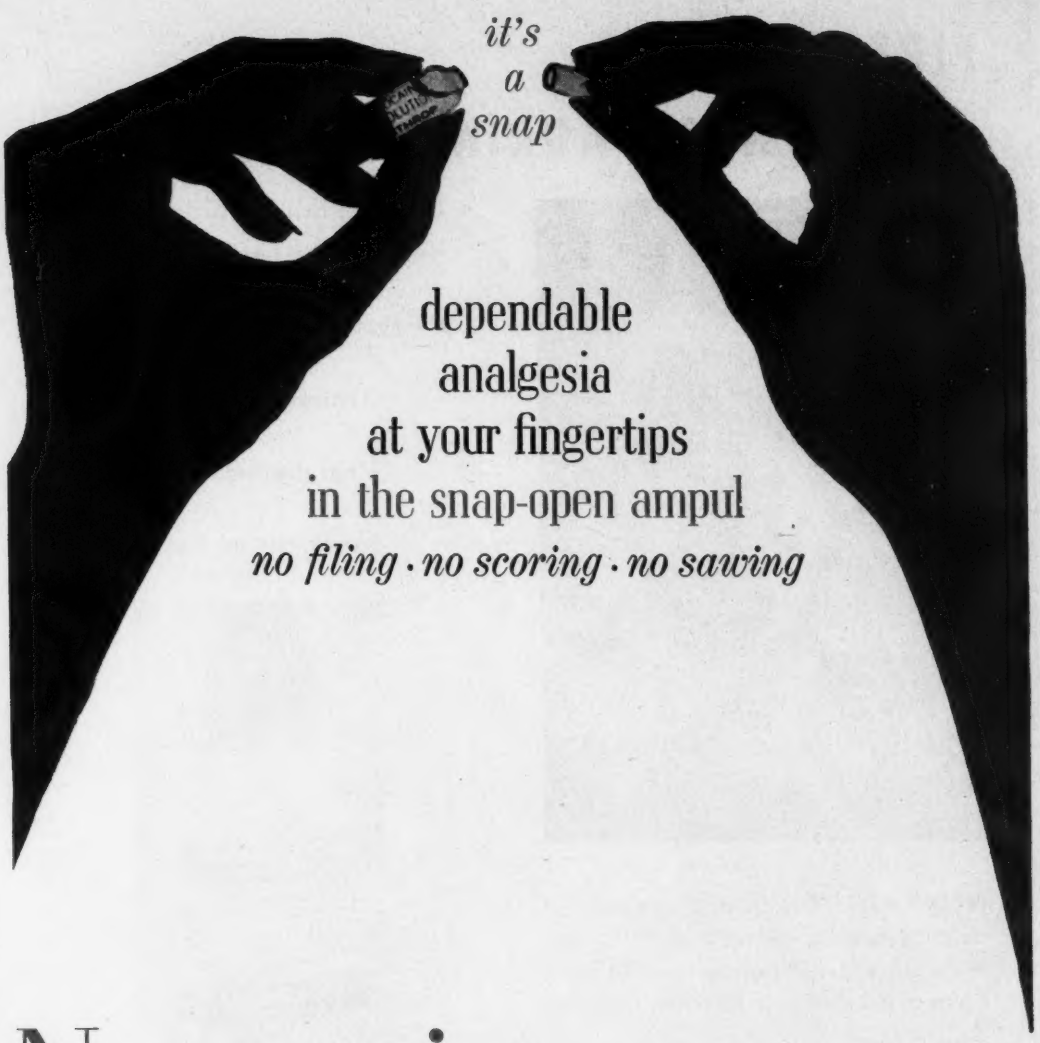

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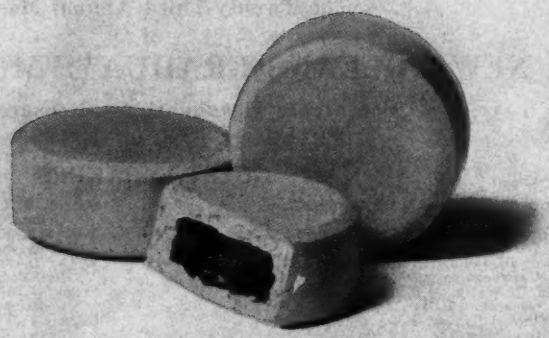

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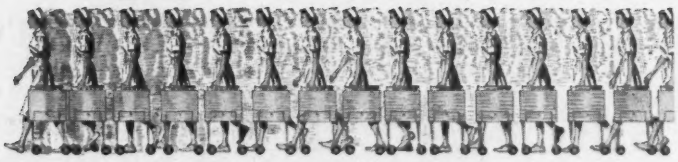

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POVAN SUSPENSION is administered orally in a single dose. In small children, the dose is equivalent to 5 mg. pyrvinium base per Kg. of body weight.

For convenience, a 5-cc. teaspoonful per 22 pounds (10 Kg.) of body weight may be recommended. For example, a 54-pound child would receive somewhat less than 3 teaspoonfuls of the Suspension.

Adults also may be given **POVAN SUSPENSION** according to the same dosage schedule.

Note: Parents and patients should be informed that **POVAN SUSPENSION** will color the stools a bright red and that, if spilled, will stain.

Supplied: **POVAN SUSPENSION** is available as a pleasant-tasting, strawberry-flavored suspension containing the equivalent of 10 mg. pyrvinium base per cc., in 2-oz. bottles.

(1) Beck, J. W.; Saavedra, D.; Antell, G. J., & Tejeiro, B.: Am. J. Trop. Med. 8:349, 1959.

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1. Bodi, T., and Levy, H.: Clinical report, cited with permission. 2. Wetzler, R. A., and Phillips, R. M.: Clinical report, cited with permission. 3. Prigot, A.: Clinical report, cited with permission. 4. Gosline, E., *et al.*: *Am. J. Psychiat.* 115:939 (April) 1959. 5. Turvey, S. E. C.: Clinical report, cited with permission.

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Tetracycline-Triple Sulfa Combination (TETREX® c̄ T/S) in the Treatment of INFECTION

It is generally agreed that it is ideal to withhold antibiotic and chemotherapeutic drugs until after sensitivity tests show which antibacterial agent will be most effective. But very often, in actual practice, the physician knows that delay in starting antibacterial treatment may be detrimental to the welfare of his patient. He must then select the therapy to meet the most serious and immediate threats to the patient.

Why Combination Therapy?

Certain infections do not respond as well to a single agent as to a combination. *Hemophilus influenzae* infections, which are frequent in children, are a particularly serious threat to infants and children up to about 3 or 4 years of age since they have not yet built up any appreciable immunity. Serious complications such as influenzal pneumonia, empyema, or meningitis may develop, especially in this age group. In fact, except for those periods when meningococcal meningitis is epidemic, *H. influenzae* is the most frequent cause of meningitis.[1] This gram-negative organism is highly susceptible both to the tetracyclines and to the sulfonamides. Even in severe infections, therapeutic failure can be virtually eliminated by giving sulfonamides plus tetracycline.[1] These two agents together constitute the treatment of choice, and give better results than either alone.[2]

Sulfonamides remain the drugs of choice for all meningococcal infections, including meningitis. They readily penetrate the blood-brain barrier and pass into the cerebrospinal fluid in good concentrations.[3] In treating overwhelming meningococcal infections, and complicating infections of the upper respiratory tract caused by other organisms, the addition of tetracycline to sulfas can be valuable.[4]

In recent years the sulfonamides have again been prescribed more and more frequently. In certain serious infections, better results can be obtained with a combination of antibiotic and sulfonamide than with either drug alone (e.g., severe pneumococcal pneumonia or pneumococcal meningitis[5]). Furthermore, mixed infections, to which young children are particularly susceptible, often respond only to combination therapy such as tetracycline with sulfonamides (TETREX c̄ T/S).

Why Triple Sulfas?

Some sulfonamides, though therapeutically useful, frequently crystallize and cause renal damage. Sulfonamide mixtures are designed to prevent this effect. It is known that different substances can coexist in solution without interfering with each other's solubility. In such a solution each component behaves as if it alone were present. Thus, a much larger total amount of sulfonamide can exist in the urine without precipitating if a mixture is administered than if the same amount of only one compound is given.

Similarly, there is less danger of hypersensitivity with mixtures. The incidence of sensitization varies directly with the dosage and is limited to the particular sulfa given. Simultaneous use of several sulfa compounds, each in partial dosage, tends to keep each drug below its own sensitization level.[3] As with all sulfonamides, it is advisable to check for possible blood dyscrasias, rash, or renal toxicity during extended administration.

TETREX c̄ T/S, by combining only 167 mg. each of sulfadiazine, sulfamerazine, and sulfamethazine, practically eliminates serious renal damage and sensitization reactions due to sulfonamides while retaining the therapeutic efficacy of the total dose.

TETREX c̄ T/S can be administered with confidence in all severe and mixed infections due to tetracycline-sensitive and sulfonamide-sensitive organisms, including infections of the upper respiratory, urinary, and gastrointestinal tracts.

References: 1. Alexander, H. E.: The hemophilus group. In: Dubois, R. J.: Bacterial and Mycotic Infections of Man. Ed. 3, Philadelphia, J. B. Lippincott Co., 1958, p. 470ff. 2. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, pp. 1322-1323. 3. Beckman, H.: Drugs — Their Nature, Action, and Use. Philadelphia, W. B. Saunders Co., 1958, pp. 527-528. 4. Dingle, J. H.: Meningococcal infections. In: Cecil, R. L., and Loeb, R. F.: A Textbook of Medicine. Ed. 9, Philadelphia, W. B. Saunders Co., 1955, p. 196ff. 5. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, p. 1308.

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Each 5 ml. teaspoonful contains:

Tetracycline (ammonium polyphosphate buffered equivalent to tetracycline HCl activity)	125 mg.
Sulfadiazine	167 mg.
Sulfamerazine	167 mg.
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Thanks to your treatment and the help of Deprol, her depression is relieved and her anxiety and tension calmed. She eats well, sleeps well, and can return to her normal activities.

.as it calms anxiety!

Deprol helps balance the mood by lifting depression as it calms related anxiety

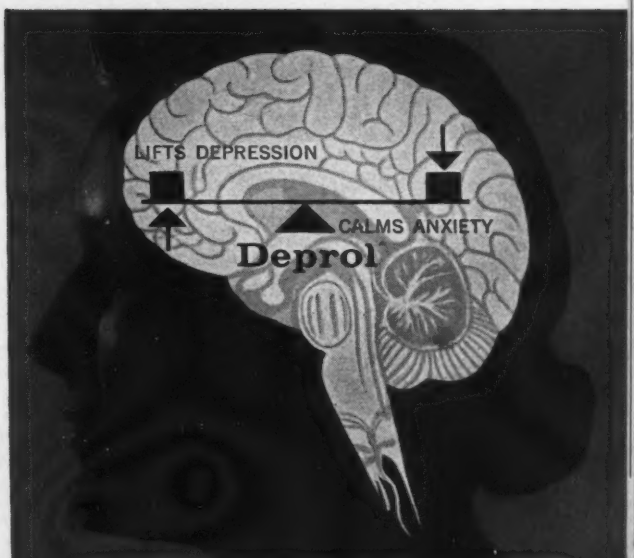
No "seesaw" effect of amphetamine-barbiturates and energizers

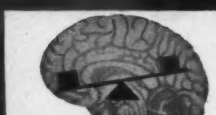
While amphetamines and energizers may stimulate the patient—*they often aggravate anxiety and tension.* And although amphetamine-barbiturate combinations may counteract excessive stimulation—*they often deepen depression.*

In contrast to such "seesaw" effects, Deprol lifts depression as it calms anxiety—both at the same time.

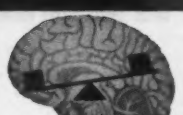
Safer choice of medication than untested drugs

Deprol does not produce hypotension, liver damage, psychotic reactions or changes in sexual function.





AMPHETAMINES AND ENERGIZERS may stimulate the patient, but often increase anxiety and tension.



AMPHETAMINE-BARBITURATE combinations may control overstimulation but may deepen depression.

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DOSAGE: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.

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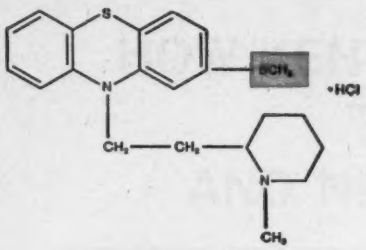

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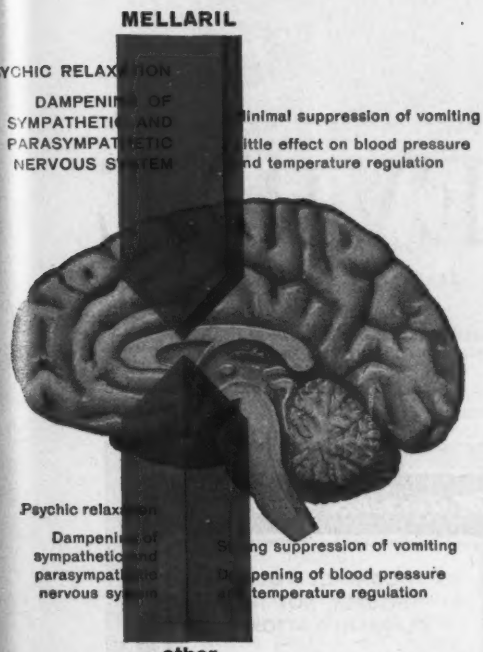

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MODERATE—where agitation exists in psychoneuroses, alcoholism, intractable pain, senility, etc.	25 mg. t.i.d.	50-200 mg.
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CHILDREN: BEHAVIOR PROBLEMS IN CHILDREN	10 mg. t.i.d.	20-40 mg.

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*Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959

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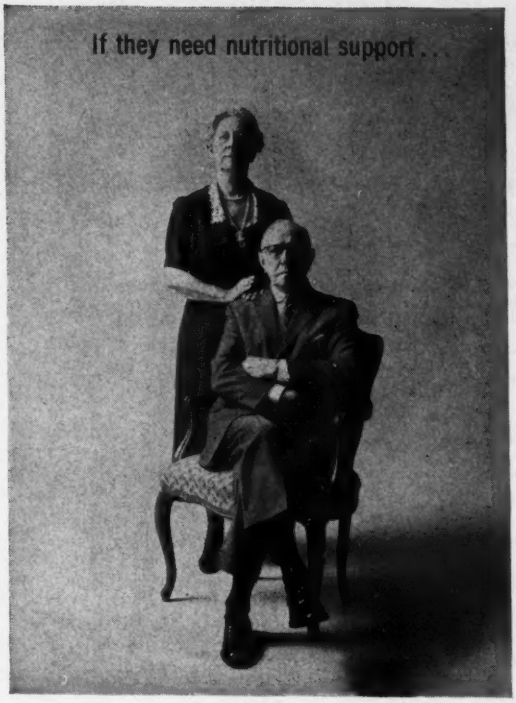

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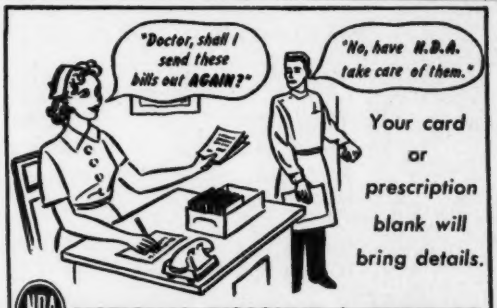

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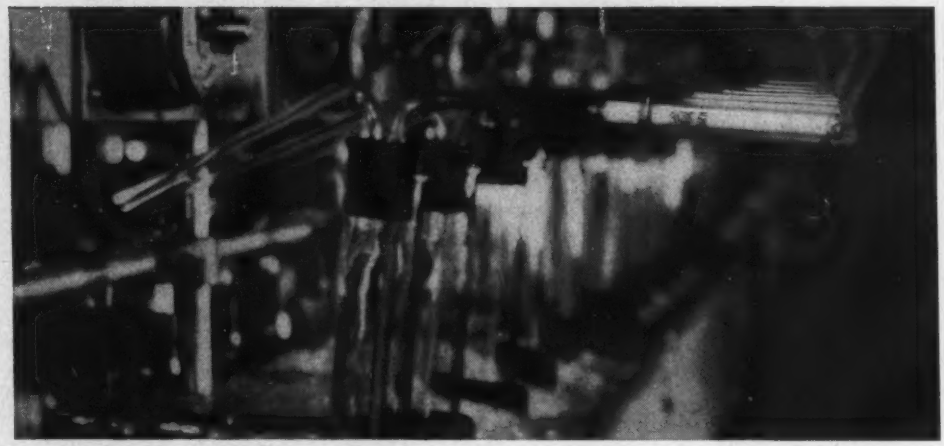

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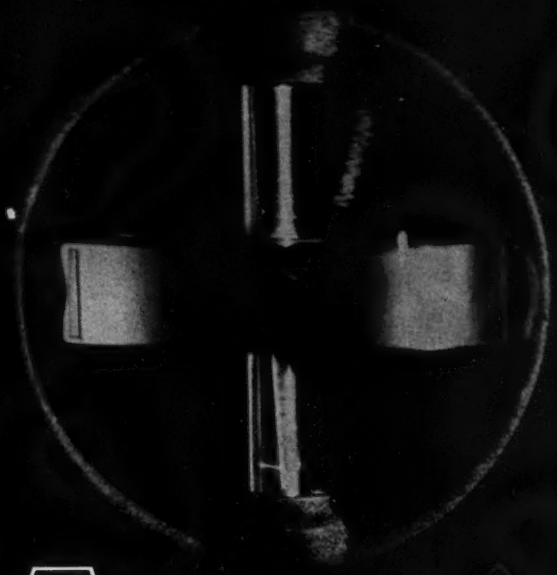

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References: 1. Feinberg, S.M., Feinberg, A.R., and Fisherman, E.W.: *J.A.M.A.* 167:58 (May 3) 1958. 2. Epstein, J.I. and Sherwood, H.: *Connecticut Med.* 22:822 (Dec.) 1958. 3. Friedlaender, S. and Friedlaender, A.S.: *Antibiotic Med. & Clin. Ther.* 5:315 (May) 1958. 4. Segal, M.S. and Duvenci, J.: *Bull. Tufts North East M. Center* 4:71 (April-June) 1958. 5. Segal, M.S.: Report to the A.M.A. Council on Drugs, *J.A.M.A.* 169:1063 (March 7) 1958. 6. Sherwood, H. and Cooke, R.A.: *J. Allergy* 28:97 (Mar.) 1958. 7. Duke, C.J. and Oviedo, R.: *Antibiotic Med. & Clin. Ther.* 5:710 (Dec.) 1958. 8. McGavack, T.H.: *Clin. Med.* (June) 1958. 9. Freyberg, R.H.; Berntsen, C.A., and Hellman, L.: *Arthritis and Rheumatism* 1:215 (June) 1958. 10. Hartung, E.F.: *J.A.M.A.* 167:973 (June 21) 1958. 11. Hartung, E.F.: *J. Florida Acad. Gen. Pract.* 8:18, 1958. 12. Zuckner, J.; Ramsey, R.H.; Caciolo, C., and Gantner, G.E.: *Ann. Rheum. Dis.* 17:398 (Dec.) 1958. 13. Appel, B.; Tye, M.J., and Leibsohn, E.: *Antibiotic Med. & Clin. Ther.* 5:716 (Dec.) 1958. 14. Kalz, F.: *Canad. M.A.J.* 79:400 (Sept.) 1958. 15. Mullins, J.F., and Wilson, C.J.: *Texas State J. Med.* 54:648 (Sept.) 1958. 16. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: *J.A.M.A.* 167:959 (June 21) 1958. 17. DuBois, E.F.: *J.A.M.A.* 167:1590 (July 26) 1958. 18. McGavack, T.H.; Kao, K.T.; Leake, D.A.; Bauer, H.G., and Berger, H.E.: *Am. J. Med. Sc.* 236:720 (Dec.) 1958. 19. Council on Drugs: *J.A.M.A.* 169:257 (Jan. 17) 1959. 20. Rein, C.R.; Fleischmajer, R., and Rosenthal, A.R.: *J.A.M.A.* 165:1821 (Dec. 7) 1957.

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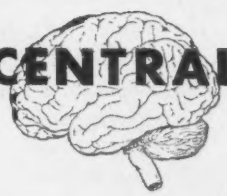

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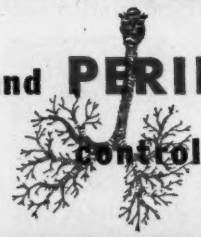

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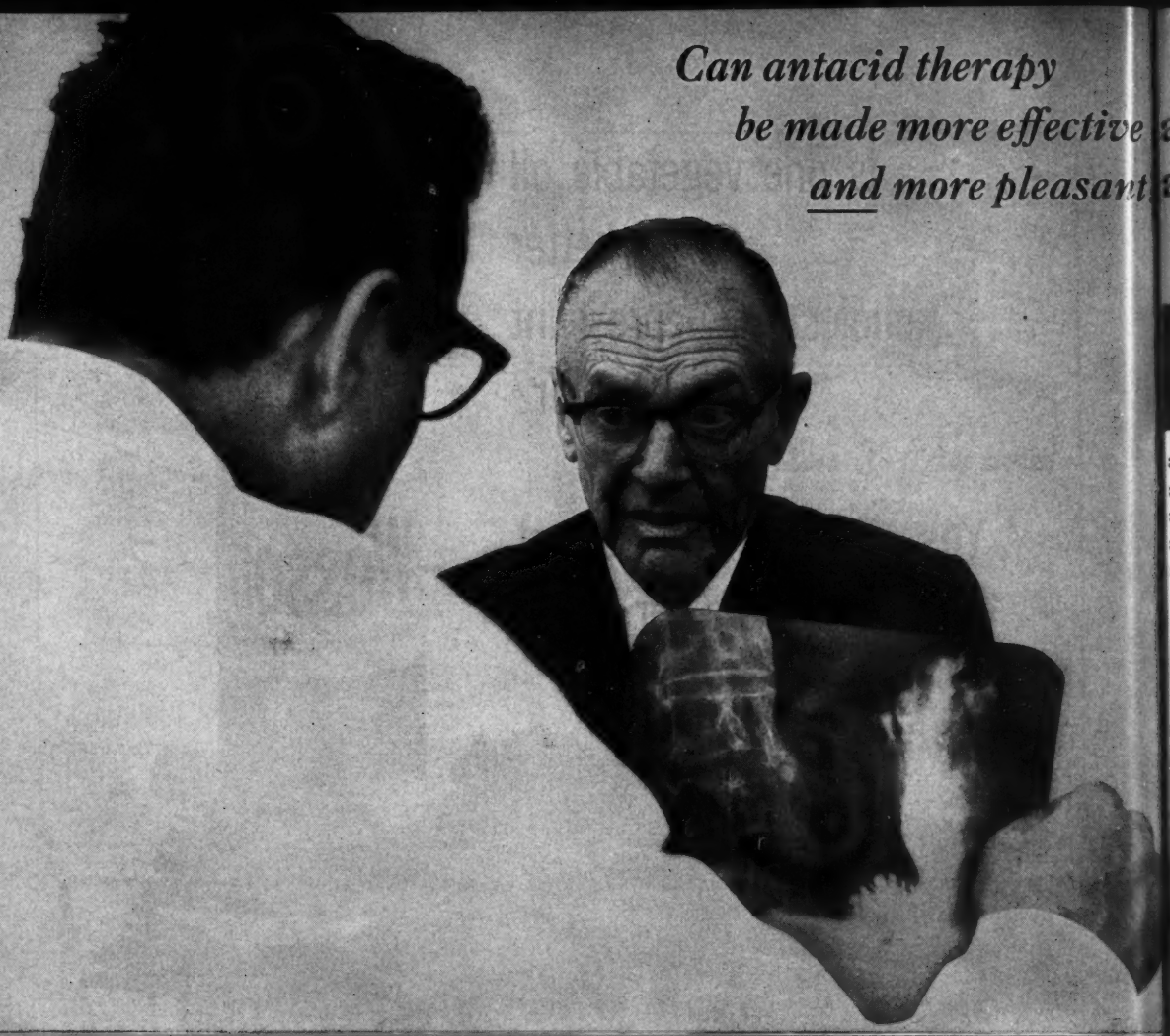

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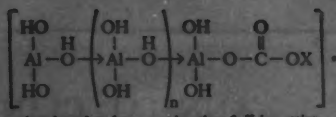

• HEXITOL

a is at least 1 and averages less than 6. X is a cation.

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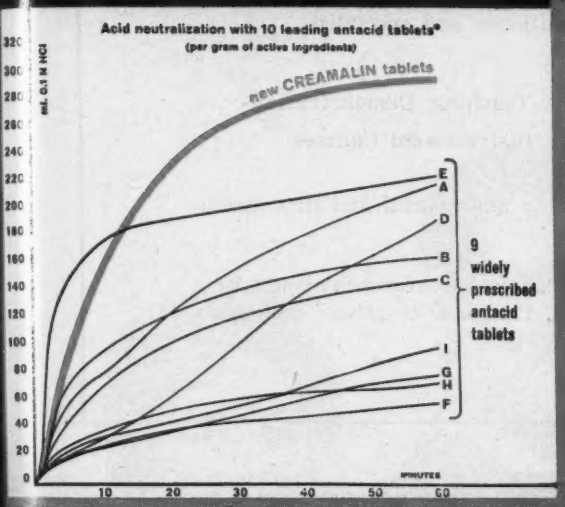
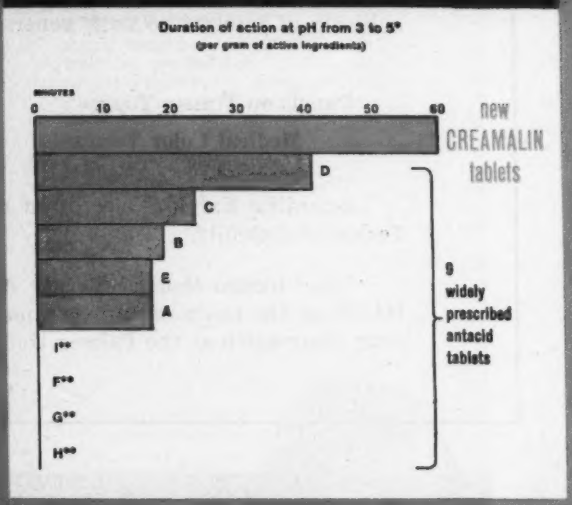
Quicker Relief • Greater Relief



Tablets were powdered and suspended in distilled water in a constant temperature container (37°C) equipped with mechanical stirrer and pH electrodes. Hydrochloric acid was added as needed to maintain pH at 3.5. Volume of acid required was recorded at frequent intervals for one hour.

CREAMALIN NEUTRALIZES *MORE* ACID *LONGER*

More Lasting Relief



*Hinsel, E. T., Jr., Fisher, M. P. and Tainter, M. L.: A new highly reactive aluminum hydroxide complex for gastric hyperacidity. To be published.
**pH stayed below 3.

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Riboflavin (B_2)	5 mg.
Niacinamide	15 mg.
Folic Acid	1 mg.
Pyridoxine HCl (B_6)	0.5 mg.
Ca Pantothenate	5 mg.
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relief comes fast and comfortably

–does not produce autonomic side reactions
–does not impair mental efficiency, motor control, or normal behavior.

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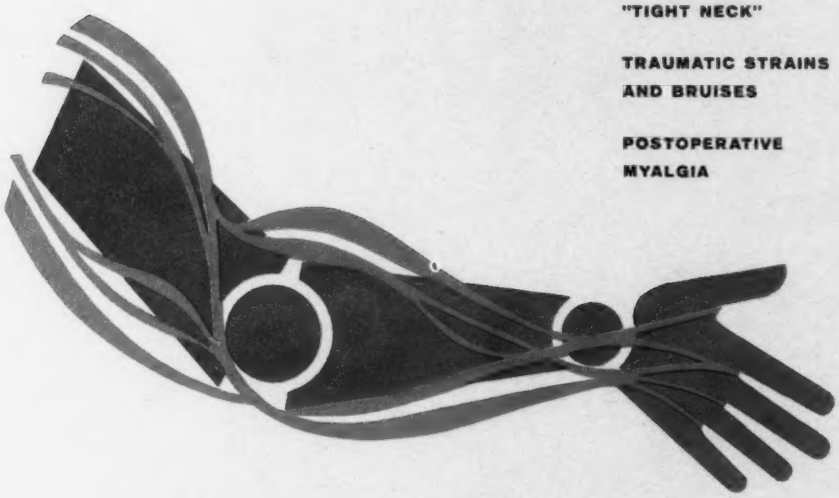

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■ More specific than salicylates ■ Less drastic than steroids

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EASY TO USE. Usual adult dose is one 350 mg. tablet 3 times daily and at bedtime.

SUPPLIED: Bottles of 50 white coated 350 mg. tablets.
Literature and samples on request.

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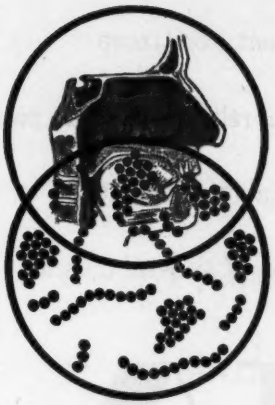

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Trisulfapyrimidines, U.S.P. .....0.5 Gm.

Dosage:

Adults—2 to 4 tablets or tsp. initially, followed by 2 tablets or tsp. every 4 to 6 hours until the patient has been afebrile 3 days. *Children 8 to 12* – 2 tablets or tsp. initially, followed by 1 tablet or tsp. every 6 hours. *Children under 8*—dosage according to weight.

The palatability, convenience and effectiveness of the Suspension make it especially suitable for children and for those older patients who prefer liquid medication.

References: 1. Cecil, R. L., et al.: J.A.M.A. 124:8 (Jan. 1) 1944. 2. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 3. Beckman, H.: Drugs, Their Nature, Action & Use, Saunders, Philadelphia, 1958, p. 527.

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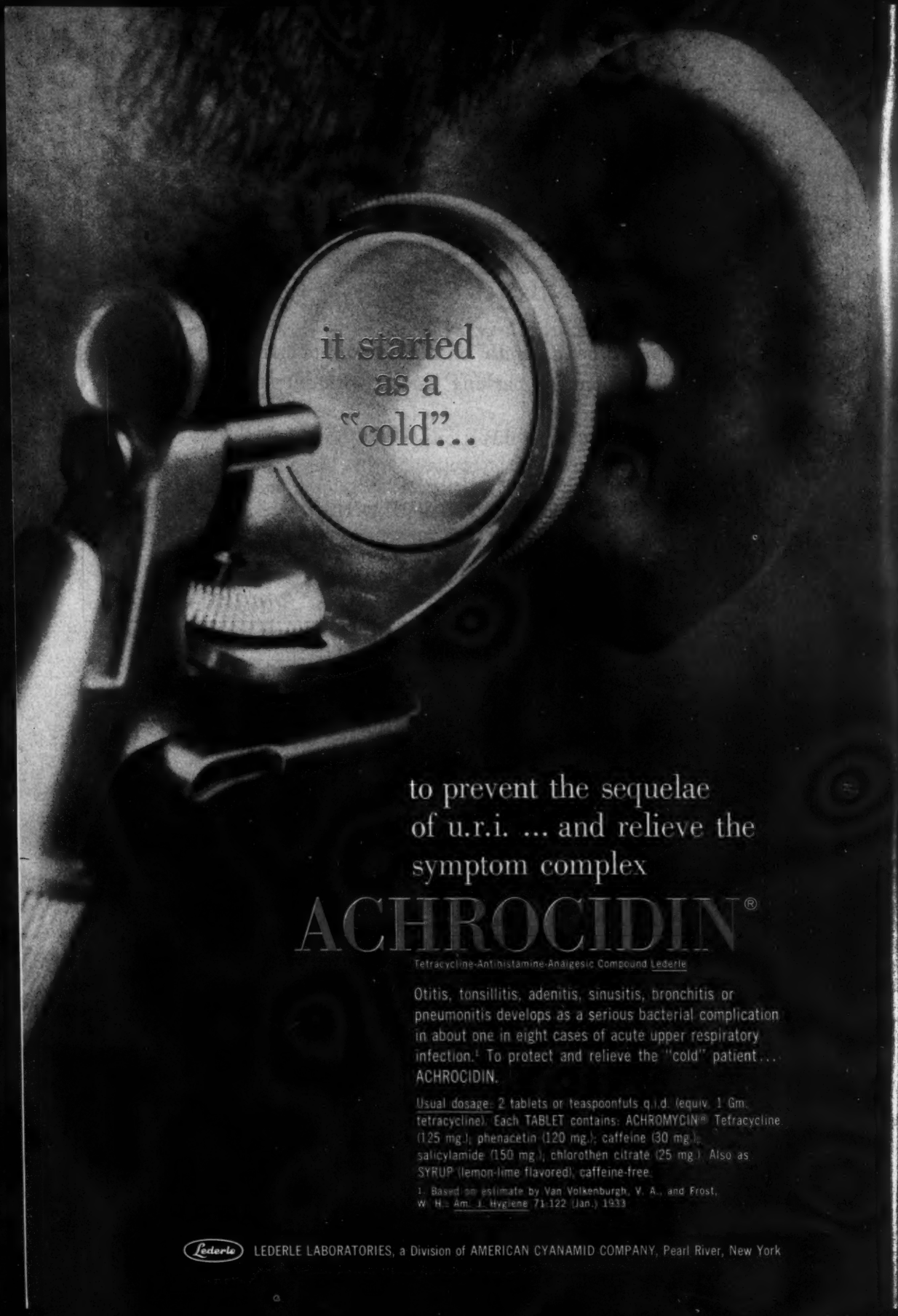

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1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

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Clinical reports on Dartal: 1. Edisen, C. B., and Samuels, A. S.: A.M.A. Arch. Neurol. & Psychiat. *80*:481 (Oct.) 1958. 2. Ferrand, P. T.: Minnesota Med. *41*:853 (Dec.) 1958. 3. Mathews, F. P.: Am. J. Psychiat. *114*:1034 (May) 1958.

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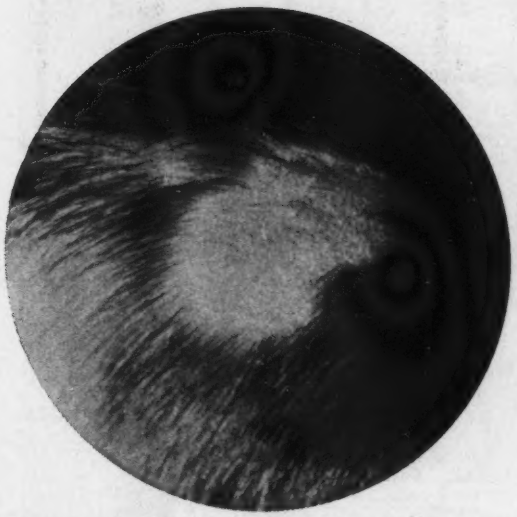

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After FULVICIN: Normal, new hair growth after 6 weeks of oral therapy.

Photos courtesy of M. M. Nierman, M.D., Calumet City, Ill.

Lesions clear, cultures become negative in

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tinea cruris: 4 to 6 weeks[1]
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first *oral* fungistat to penetrate keratin *from the inside*... acts to check invading ringworm fungi *(Microsporum, Trichophyton, Epidermophyton)*...usually well tolerated, side effects rare in therapeutic doses.

For complete information about dosage, indications and precautions consult Schering Statement of Directions.

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1. Robinson, H. M., Jr., *et al.*: Griseofulvin, Clinical and Experimental Studies, A.M.A. Arch. Dermat., in press.

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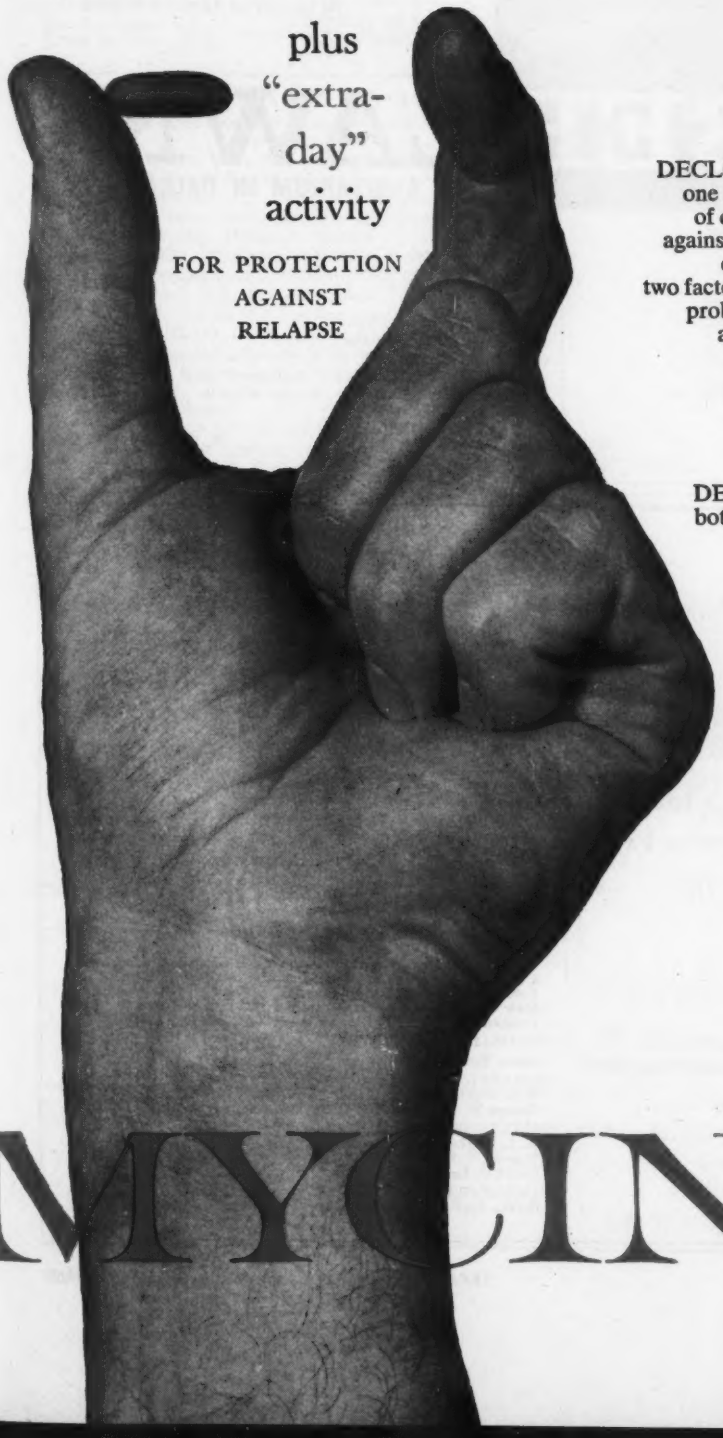

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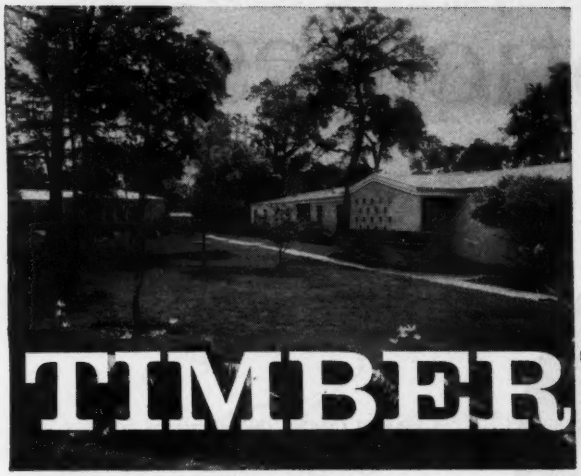

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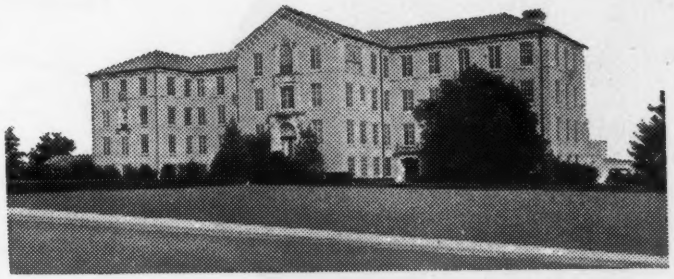

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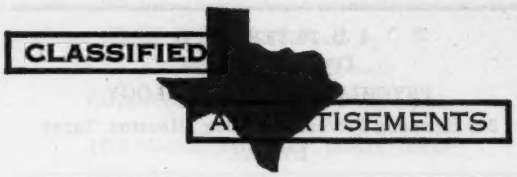

★ Physicians Wanted

WANTED—EENT department head in six-doctor clinic in Central Texas. Ophthalmologist preferable. Board certification desirable, not necessary. Address Box 878, care Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED—General practitioner preferably under 40 years of age; capable of handling some general surgery to associate with 3 active and busy physicians in clinic. Salary guarantee first year, then percentage, to locate in Texas city over ½ million population. State full qualifications in application. Reply to Box 220, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED— General Practitioner for established practice of deceased physician. Office available in good clinic. Equipment for reasonable rental or purchase. Location: prosperous southeast Texas town of 3,400, large trade area, near Houston, San Antonio, Austin. Details supplied. Write Box 245, Texas State Journal of Medicine 1801 North Lamar Blvd., Austin, Texas.

WANTED: Associate in modern clinic. Will consider general surgeon, Pediatrician, internal medicine, E.E.N.T. or G.P. Salary open. Address letters to Box 252, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED: General Practitioner: competent, reliable, pleasing personality, interested in becoming associated with established busy, modern clinic. Pediatrics, obstetrics, medicine and general surgery. South Central Texas. Salary open. Box 255, Texas State Journal of Medicine. 1801 North Lamar Blvd., Austin, Texas.

PSYCHIATRY RESIDENCY—Three year approved. 1259-bed VA Hospital closely affiliated with medical school. 400-bed acute Psychiatric Service which includes female ward, Neurology, consultation service, follow-up clinic. Mental hygiene clinic. Extensive research facilities. Salary $3250-$4165. Available under career program $6505-$9890. Write Box 281, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

PEDIATRICIAN wanted to take over 7-year-old active practice in Southwest Houston. Present pediatrician leaving practice January 1, for two-year special training. Details to be worked out. Reply to box number 291, Texas State Journal of Medicine, 1801 North Lamar Boulevard, Austin, Texas.

WANTED: Young general practitioner for association with doctor in well-established practice. Fully equipped clinic in Gulf Coast Town. Guaranteed salary while on trial basis with potential full partnership if qualified. Reply box number 335, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED: Internist to join old established group in town of 10,000 population in West Texas. Need not be Board certified but with adequate residency training. Write Box 301, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED: Surgeon to join old established group in town of 10,000 population in West Texas. Need not be Board certified but with adequate residency training. Write Box 302, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

GENERAL PRACTITIONER WANTED to take over busy general practice in Central Texas. Complete facilities and equipment for 1 or 2 G.P.'s. Contact Box 297, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

GENERAL PRACTITIONER WANTED—Odessa, Texas; population 96,000. To occupy office in Sherwood Medical Center (not a clinic). Center is of white brick construction; mall type design; perfect arrangement; solo practice; for information and brochure write or call D. C. Harrill, 1813 East 8th Street, FE 2-1401, Odessa, Texas.

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WANTED: INTERNIST to fill vacancy with well established specialists in Dallas (Oak Cliff). One would be busy in this location almost from the first, practice is on independent basis (no clinic). Contact box number 307, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

ASSOCIATE WANTED: Panhandle of Texas, modern clinic, busy general practice. Excellent hospital available. Salary first year, if needed. Write box 309, Texas State Journal of Medicine, 1801 North Lamar Boulevard, Austin, Texas

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PEDIATRICIAN WANTED—To occupy space in starting group clinic. Located in fast growing residential area in northeast Dallas. Write Box 315, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED: Internist and one General Practitioner for group practice in well-established 4-man clinic in fast growing West Texas city. Excellent hospital adjoining clinic. Excellent starting salary. Contact Charles A. Weeg, Administrator, Howard County Hospital Foundation, Box 949, Big Spring, Texas.

ASSOCIATE WANTED to join general practitioner in new clinic-hospital combination. Prefer to be capable of doing some surgery. Beginning salary $18,000 or percentage. Will consider future partnership. Contact M. A. Childress, M.D., Goldthwaite, Texas.

Excellent opportunity for TWO DOCTORS to take the place of two leaving for residencies. Serve area of 12,000 people, $35,000 net each yearly. Modern brick clinic building completely furnished for sale to one or two men. Desire to sell equity in building, equipment, practice. Reply to Box Number 321, Texas State Journal of Medicine, 1801 N. Lamar Blvd., Austin, Texas.

WANTED: Young general practitioner, Texas license, to associate with two physicians in well-established clinic. Remuneration subject to ability and effort. Write Box 546, Seminole, Texas.

STAFF physician for San Antonio State Tuberculosis Hospital, San Antonio, Texas. Salary from $10,600.00, depending on qualifications, paid vacation, retirement plan, sick leave. Write Superintendent, P. O. Box 7206, Hackberry Station, San Antonio 10, Texas.

WANTED—General practitioner for established practice of recently deceased physician. Fully equipped, air-conditioned, ten-room clinic in town of 5,000 plus rural. Will lease or sell. If interested, contact Mrs. Robert Cumming, 217 Madison Street, McGregor, Texas.

PSYCHIATRY RESIDENCIES—Southwestern Medical School, Parkland Memorial Hospital 3-year approval; program features inpatient, outpatient, psychosomatic, and child experiences in teaching and research setting; special general practitioner fellowships are available. Direct inquiries to: R. L. Stubblefield, M.D., Medical School, 5323 Harry Hines Blvd., Dallas, Texas.

WANTED—Physician to take over office and general and obstetrical practice. Location: Rio Grande Valley; population 10,000. Constant practice 21 years to date. Office fairly well equipped. Terms: monthly payment basis or outright. Present physician intends to specialize. Reply to Box 218, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED—Hard working, ambitious, general practitioner for staff of Modern County Hospital in Northwest Texas, community of 2,800 and county of 6,500 without a resident M.D. New County Hospital to be available within next 12 months, excellent opportunity for general practice. If interested, please submit brief outline of background. Reply to Box 324, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

WANTED IMMEDIATELY—House physician Railroad General Hospital. Room, board, many other benefits. Starting monthly salary over $1,000.00. Requirements: U. S. citizenship, licensed or eligibility Texas license, general surgical experience. Write, wire, call collect: Chief Surgeon, T & P Hospital, Marshall, Texas. Telephone WE 4-4313.

EXCELLENT OPPORTUNITY FOR UROLOGIST—Suite 1, in Sherwood Medical Center is now available, this suite is designed for urologist by a urologist and is in our opinion one of the best located offices in the Center. If you would like to practice in a town of 100,000 residents with the town still growing, contact D. C. Harrill at 1813 East 8th Street, Phone FE 2-1401, Odessa, Texas.

YOUNG DOCTOR desired for practice with 39-year-old physician in Fort Worth-Dallas area small town. Hospital and clinic for general practice and obstetrics. Excellent possibilities for future partnership. Inquiries may be directed to Grapevine Clinic and Hospital, 1015 West Northwest Highway, Grapevine, Texas.

WANTED—Psychiatrist, salary to $15,000. State minimum security correctional facility in highly desirable area. Write Chief Medical Officer, California Men's Colony, Los Padres, California.

OFFICE SPACE for Spanish-speaking doctor. In a good location in city of 150,000 population. Many patients from the city and surrounding area. The two doctors now in office leaving for special training. Reply to Box 328, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

GENERAL PRACTICE group seeking qualified G. P. to take over practice in Northwest Texas county seat community, with new county hospital to be completed in next 12 months. Write Box 329, Texas State Journal of Medicine, 1801 North Lamar Boulevard, Austin, Texas.

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OPENINGS—For Physicians, age 25-45. Salary range from $10,000 to $12,500 per year, depending upon qualifications and experience. Texas license required. Training in Psychiatry not essential but desirable. Work primarily in Medical & Surgical Hospital. Participation in State Retirement Program, paid vacations, holidays, and sick leave. Apply Personnel Office, Wichita Falls State Hospital, Wichita Falls, Texas.

G. P. WANTED—To associate with General Practitioner. Write: Melvin Anchell, M.D., 9129 East Houston Road, Houston 28, Texas.

YOUNG DOCTOR needed in Central Texas town of McGregor. Good opportunity in this 4,000 population community. Have good churches and schools. Office space available adjoining drug store. Contact M. H. Evers, Pharmacist, P. O. Box 638, McGregor, Texas.

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YOUNG GENERAL PRACTITIONER with 5 years of general practice experience seeks position as salaried associate with a general practice group or as a general practice resident in a small hospital. Married, veteran, and will be available after January 1, 1960. Contact Box 314, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

AVAILABLE in 60 days. General Surgeon, age 34, Board Eligible. Experienced in major trauma and orthopedic surgery. Desires Texas location. Service obligation completed. Write to Box Number 318, Texas State Journal of Medicine, Austin, Texas.

BOARD ELIGIBLE internist, trained in allergy, gastroenterology. Age 46, married, veteran. Seeks location or association. Reply to Box Number 320, Texas State Journal of Medicine, Austin, Texas.

SITUATION WANTED—OPHTHALMOLOGIST: Young, married, Board certified. Excellent training and references. Desires association with another ophthalmologist or Clinic Group. Prefer Oklahoma, Texas, or Louisiana. Write to Box 323, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

SITUATION WANTED—Young, board certified surgeon, looking for small group or association with other young surgeon. Write to Box 325, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

ALLERGIST desires partnership or group association. Background general pediatrics and pediatric and adult allergy. Certified. Available August, 1960. Reply to Box 327, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

OBSTETRICIAN-GYNECOLOGIST—Southerner, age 35, family, veteran. M.D. John Hopkins, 1951. Completing approved residency July, 1960. Desires association with one or more OB-GYN men or group upon completion of residency. Contact Dr. R. D. Dean, 129 Colonial Circle, Jackson 6, Mississippi.

SITUATION WANTED—Two-week "Locum Tenens" in General Practice in San Antonio area for winter or spring months. Reply to Box 331, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.

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FOR SALE: EENT equipment in good-to-excellent condition. Complete list furnished if interested. Doctor retiring, location open. Reply to Box number 306, Texas State Journal of Medicine, 1801 North Lamar Boulevard, Austin, Texas.

FOR RENT IN FORT WORTH (Dentist) Jewell Clinic in desirable completely built and established suburban location has unfurnished office suite for lease for independent practice to Dentist. Reception room and receptionist would be shared. Will assist in developing practice and give lower than normal rent for first year. George W. Jewell, Jr., M.D., 5201 River Oaks, Fort Worth, Texas.

FOR RENT IN FORT WORTH (Obstetrician)—Jewell Clinic in desirable completely built and established suburban location has unfurnished office suite for lease for independent practice to OB Specialist. No other Obstetrical Doctor. Reception room and receptionist would be shared. Will assist in developing practice and give lower than normal rent for first year. Six miles from hospitals. George W. Jewell, Jr., M.D., 5201 River Oaks Blvd., Fort Worth, Texas.

FOR SALE: Slightly used x-ray with view boxes; development tank, and other accessories. Contact B. E. Pickett, Sr., M.D., 106 Pena Street, Carrizo Springs, Texas.

FOR SALE: Complete small X-ray outfit, 15 m.a. unit with tank, cassettes, hangers, grid, view-box. Write to Post Office Box 395, Pilot Point, Texas.

FOR RENT OR LEASE—Stone Clinic in medical center. Space for two physicians. Good location, 1100 Pennsylvania Avenue, Ft. Worth. Near hospitals. Entrance foyer, business office, central reception room, auxiliary reception room, laboratory, two bedrooms. Each suite consists of consultation office and two examining rooms. Reception rooms and one suite furnished. Ample parking facilities. Reply to Box Number 316, Texas State Journal of Medicine, 1801 N. Lamar Blvd., Austin, Texas.

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★ Miscellaneous

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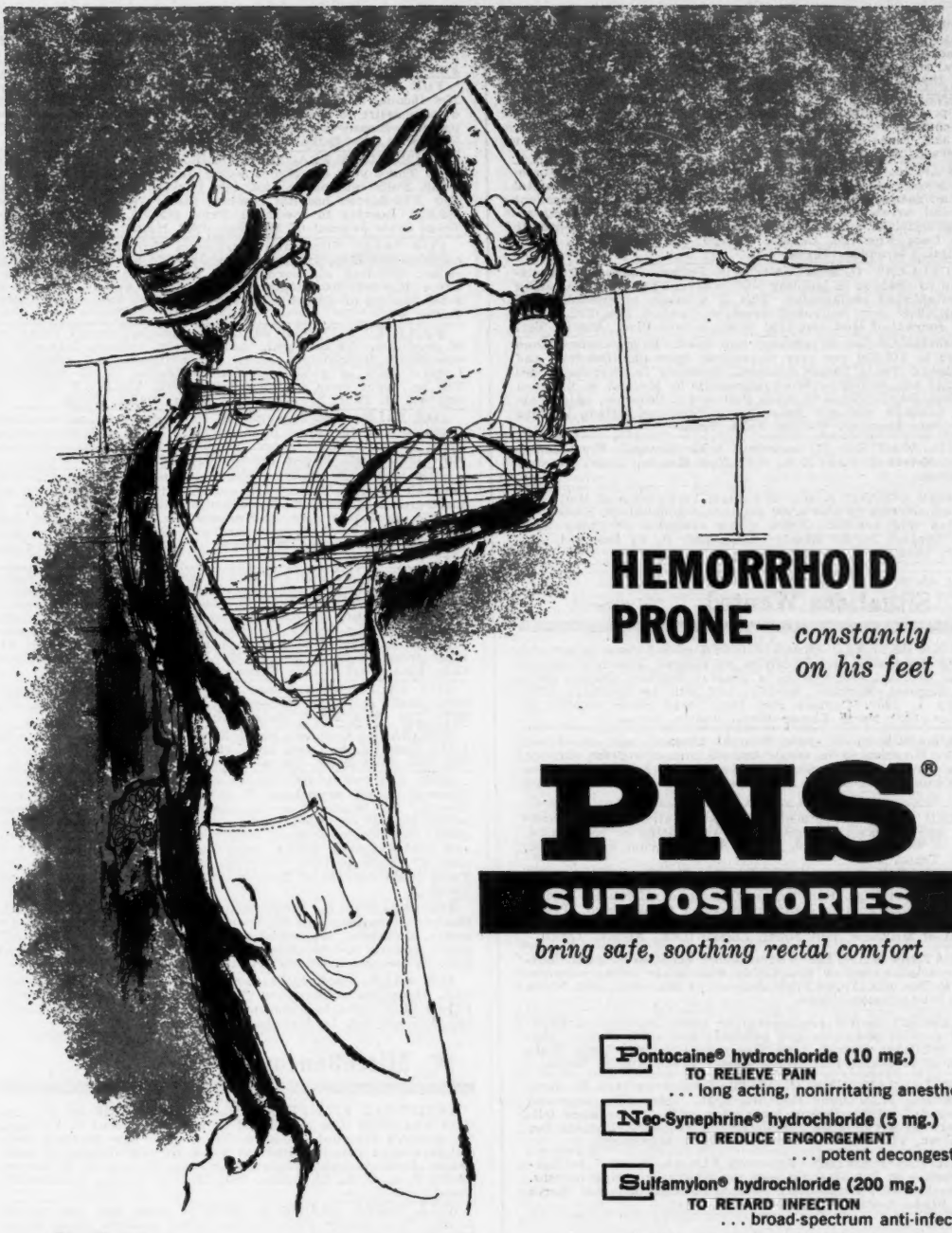
10 ROOM CLINIC: Physician needed to take over established practice in 10-room clinic in Central Texas Community, population 3,000. Will sell, lease or finance if interested. Contact Mrs. Robert Cumming, 217 South Madison, McGregor, Texas.

OFFICE suite for two M.D.'s in beautiful new Professional Building, located in fast-growing suburban Garland. Pop. 40,000. Contact James D. Wester, D.D.S., 1301 W. Garland Ave., Garland, Texas.

EXPERIENCED PHARMACIST desires space in Clinic or small hospital in Texas. Lease on percentage basis. Best references. Replies confidential. Write to Box 326, Texas State Journal of Medicine, 1801 North Lamar Blvd., Austin, Texas.



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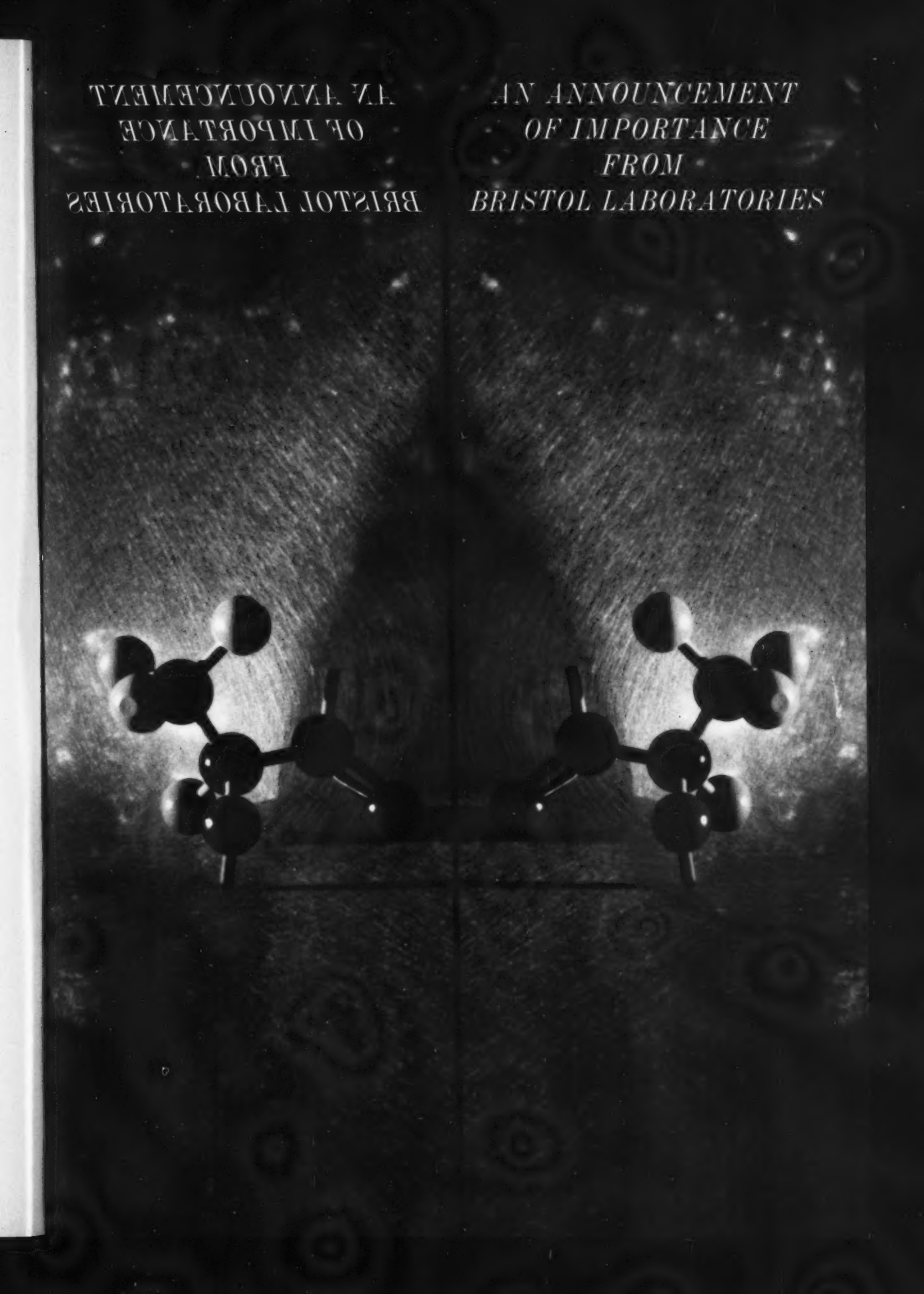

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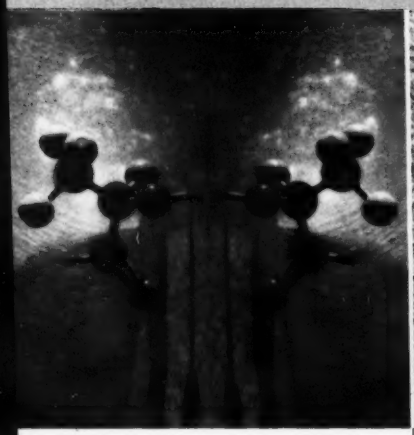
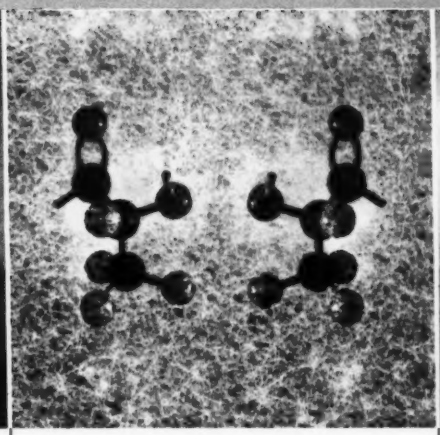
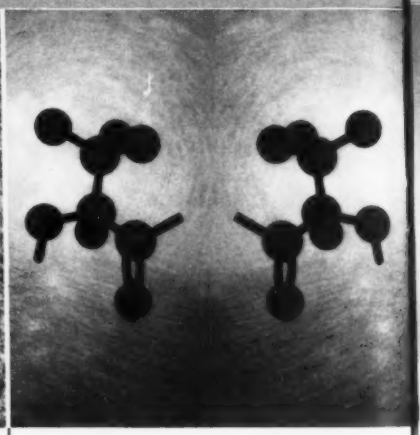






BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V

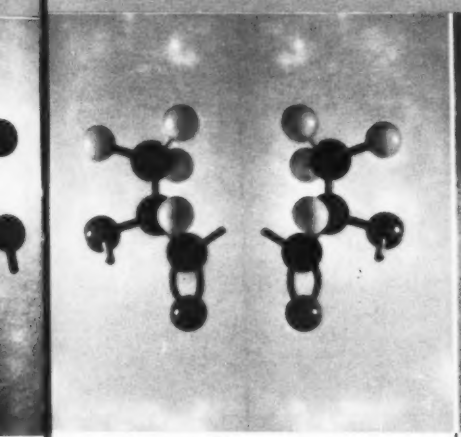
SAFER ORAL ROUTE PROVIDES HIGHER BLOOD LEVELS THAN INTRAMUSCULAR PENICILLIN G

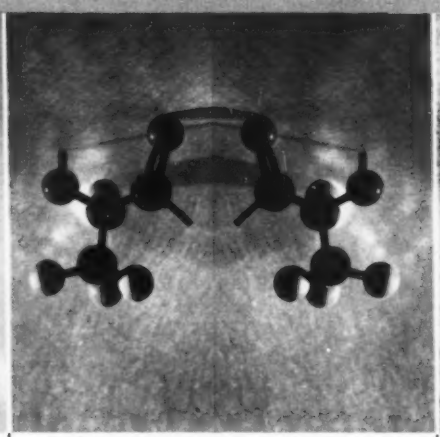
IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

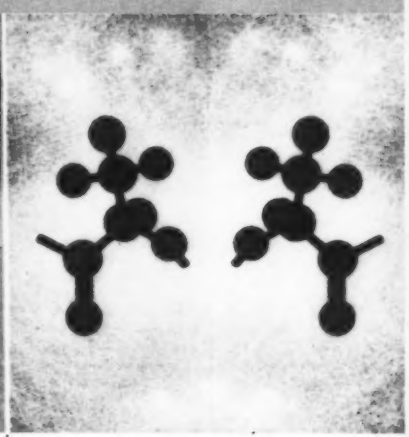
ADVANTAGES ACCOMPANY MOLECULAR ASYMMETRY

CILLIN™

POTASSIUM PENICILLIN-152







ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSE

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

MANY STAPH STRAINS MORE SENSITIVE TO SYNCILLIN

BRISTOL

ORIGIN OF A NEW SYNTHETIC PENICILLIN

In March, 1957, Dr. John C. Sheehan of the Massachusetts Institute of Technology announced the total synthesis of penicillin from common raw materials, thus solving a problem which had baffled research workers for more than 15 years. Although total synthesis was not commercially practicable, this work, sponsored by Bristol Laboratories, made possible the subsequent synthesis of new penicillins not occurring in nature. Later scientists at Beecham Laboratories in England discovered that a key intermediate (6-aminopenicillanic acid) could be produced by a fermentation process. With these achievements, large scale production of synthetic penicillins became feasible.

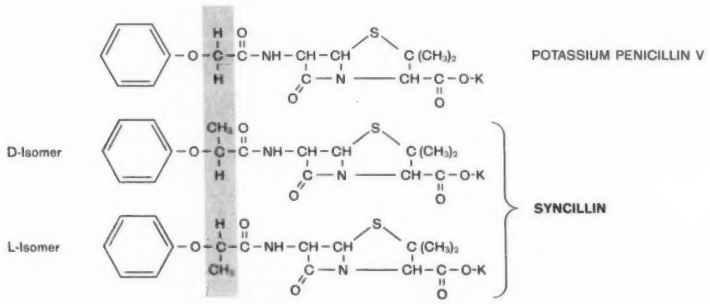
Organic chemists at Bristol then embarked upon an intensive program to develop better penicillins. Over five hundred were synthesized and underwent preliminary screening. Forty-six showed sufficient promise to warrant further investigation. Extensive microbiological, pharmacological, and clinical screening indicated that one compound, SYNCILLIN, had advantages of major importance over other penicillins.

SYNCILLIN is the N-acylation product of 6-aminopenicillanic acid and α-phenoxypropionic acid (the phenylether of lactic acid). It is freely soluble in water and remarkably resistant to decomposition by acid. The acid stability of SYNCILLIN is equivalent to that of penicillin V at pH 2 and pH 3 at 37° C.[1]

SIGNIFICANCE OF MOLECULAR ASYMMETRY AND ISOMERIC COMPLEMENTARITY

SYNCILLIN has a molecular configuration similar to penicillin V, but contains an additional CH_3 group so positioned as to render the adjacent carbon atom asymmetric. (In the formulae below, the added CH_3 group is shown in blue and the asymmetric carbon atom in red.) As a result, SYNCILLIN occurs as a mixture of two isomers.

Each isomer has been synthesized in essentially pure form and found to possess distinctive chemical and biological properties. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. As produced, SYNCILLIN is a mixture of the L-isomer and the D-isomer. As will be shown later, the antibiotic effect of the clinically available mixture, SYNCILLIN, is greater than either isomer alone against many organisms. This phenomenon is referred to here as *isomeric complementarity*.



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

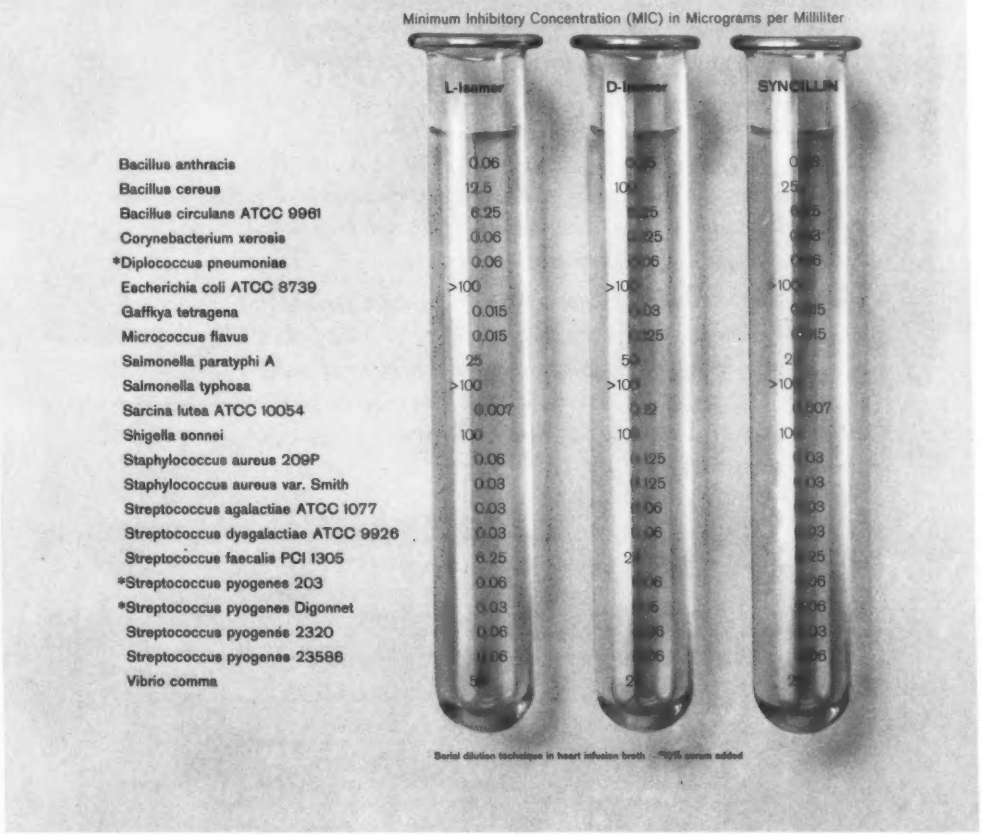
ISOMERIC COMPLEMENTARITY DEMONSTRATED IN VITRO

The *in vitro* minimum inhibitory concentration (MIC) of SYNCILLIN and of each of its two component isomers was determined for a variety of common pathogens and laboratory test organisms. As may be seen from Table 1, all three are highly effective against penicillin-susceptible staphylococci and against pneumococci, streptococci, gonococci, and corynebacteria; all are ineffective against Salmonella, *E. coli,* and other gram-negative coliform bacilli.

SYNCILLIN was more active against many of the test strains including some streptococci and staphylococci than either of its components. This demonstrates *in vitro* the phenomenon of isomeric complementarity.

TABLE 1

Minimum Concentrations of SYNCILLIN and Components Required to Inhibit a Wide Range of Bacteria



SYNCILLIN

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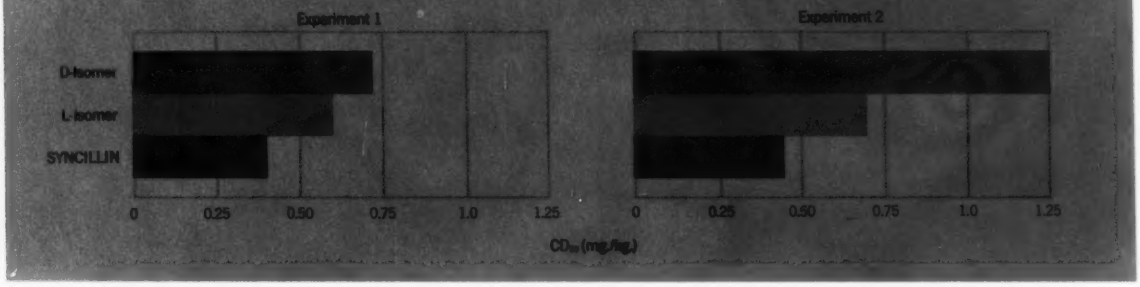
ISOMERIC COMPLEMENTARITY CONFIRMED IN VIVO

To determine the median curative dose (CD_{50}) mice were infected with 100 times the lethal dose of *Staphylococcus aureus*. Each penicillin being tested was administered intramuscularly at the same time, and the dose required to cure half the animals determined. The greater effect of the mixture of the two isomers (SYNCILLIN) is shown in two independent experiments. (See Figure 1.) Note that isomeric complementarity is thus confirmed *in vivo*.

FIGURE 1 — Median Curative Dose (CD_{50}) for *Staphylococcus aureus* (var. Smith) Infections

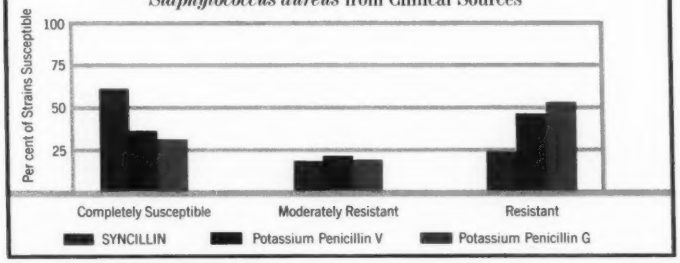


MANY STRAINS OF STAPHYLOCOCCI MORE SENSITIVE TO SYNCILLIN

SYNCILLIN has been tested against a large number of strains of *Staphylococcus aureus* isolated from clinical sources. Many organisms resistant to potassium penicillin G and potassium penicillin V proved sensitive to SYNCILLIN.

Wright[2] performed sensitivity studies on 54 strains, the majority of which were resistant or moderately resistant to penicillin V and penicillin G. Thirty-two (60%) of the strains were sensitive to SYNCILLIN, approximately twice as many as with the other penicillins. (See Figure 2.) In two-thirds of the isolates, SYNCILLIN produced inhibition at concentrations lower than those required for either of the other antibiotics. One strain was more sensitive to penicillin G.

FIGURE 2 – *In Vitro* Sensitivity of 54 Strains of Coagulase-Positive *Staphylococcus aureus* from Clinical Sources



Adapted from Wright[2]

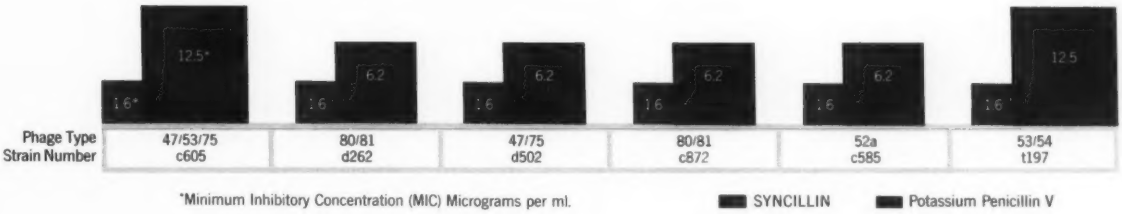
SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Of equal interest are the findings of White.[3] Six penicillin-resistant strains of staphylococci were isolated from hospital infections. None was sensitive to potassium penicillin V. All were sensitive to SYNCILLIN. (See Figure 3.)

FIGURE 3

Minimum Concentrations of SYNCILLIN Required to Inhibit
Hospital Strains of *Staphylococcus aureus* Resistant to Potassium Penicillin V

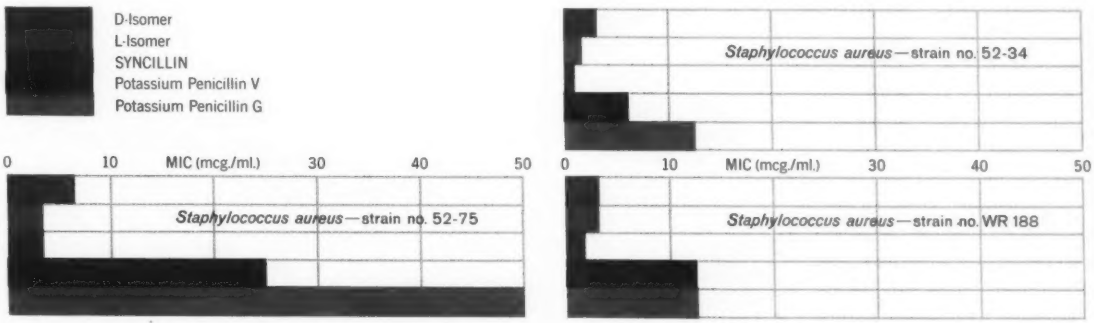


The efficacy of SYNCILLIN against the type 80/81 Staphylococcus (dangerous and widespread in hospitals) is worthy of special attention.

The complementary action of the component isomers is also seen with strains of staphylococci resistant to penicillins. Note that SYNCILLIN is more effective than either isomer against strains 52-34 and WR 188. (See Figure 4.) Against all three strains, SYNCILLIN is effective at concentrations below serum levels, while penicillins V and G are ineffective.

FIGURE 4

Minimum Inhibitory Concentrations (MIC) for Coagulase-Positive
Penicillin-Resistant Strains of *Staphylococcus aureus*



Isomeric complementarity has thus been demonstrated for:

— *certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

— *penicillin-susceptible staphylococci* in vivo *(Figure 1)*

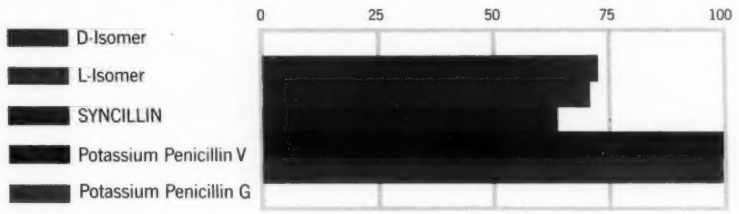
— *penicillin-resistant staphylococci* in vitro *(Figure 4)*

ISOMERIC COMPLEMENTARITY SHOWN BY REDUCED RATE OF INACTIVATION BY PENICILLINASE

Bacterial resistance to penicillin has been attributed to the action of penicillin-inactivating enzymes produced by the invading organisms.[4] As shown in Figure 5, SYNCILLIN is less affected by staphylococcal penicillinase than either of its component isomers – a further demonstration of isomeric complementarity. Further, SYNCILLIN is shown to be less inactivated by this enzyme than penicillin V and penicillin G.

Resistance to SYNCILLIN develops in a slow, step-wise manner characteristic of other penicillins, in contrast to the usually rapid development of resistance to streptomycin.

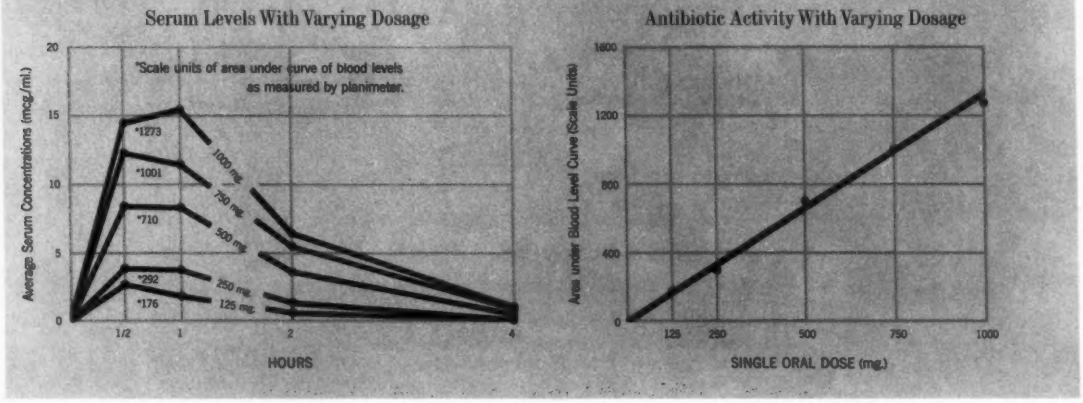
FIGURE 5—Effect of Staphylococcal Penicillinase on Different Penicillins



ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSAGE

Cronk[5] studied blood levels after administering varying amounts of SYNCILLIN. (Figure 6.) Total antibiotic activity (obtained by measuring areas under curves with a planimeter) increases rapidly as the dose is doubled. These data show that increased dosage markedly increases serum concentration and thus may enhance the drug's effectiveness.

FIGURE 6



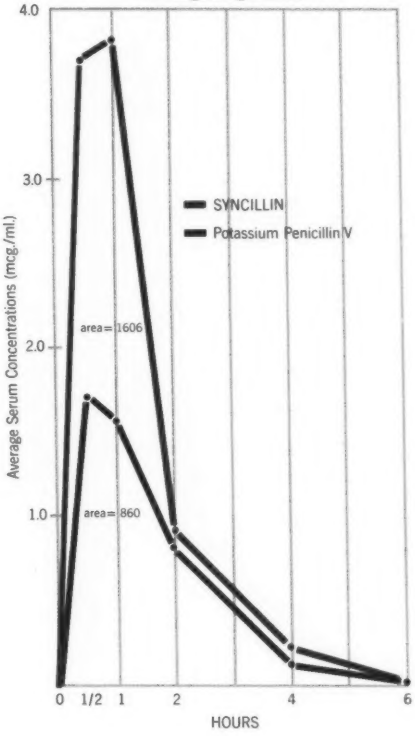
BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V AFTER ORAL ADMINISTRATION

Wright[6] performed comparative crossover blood level studies on volunteer subjects receiving equivalent amounts of potassium penicillin V and SYNCILLIN. The peak concentrations attained during the first hour after administration were twice as high with SYNCILLIN.

The total antibiotic activity as measured by the area under the curves (see Figure 7) indicates an almost 2 to 1 superiority of SYNCILLIN (1606) over potassium penicillin V (860).

The higher blood levels may be of value with organisms of only moderate penicillin-sensitivity where doubling the blood concentration may be essential for effective bactericidal action. In addition these higher levels may be necessary where there is infection in areas with a poor blood supply.[7] Under these circumstances a higher blood concentration may provide the increased diffusion pressure required to deliver adequate amounts to the tissue.

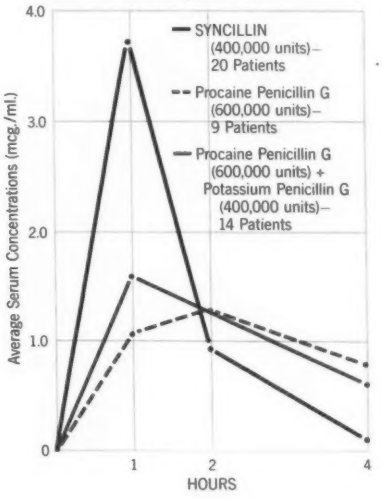
FIGURE 7
20 Subject Crossover
250 mg. Single Dose



BLOOD LEVELS MUCH HIGHER THAN WITH INTRAMUSCULAR PENICILLIN G

In addition, blood levels attained with oral SYNCILLIN[6] are much higher than those with intramuscular penicillin G.[8a, b] (See Figure 8.) Note that the level at one hour for SYNCILLIN (3.8 mcg./ml.) is more than twice as high as with procaine penicillin G, even when reinforced with potassium penicillin G (1.6 mcg./ml.). Since penicillins are *bactericidal,* these intermittent high serum levels can be clinically significant. Thus, SYNCILLIN offers the promise of superior efficacy via the safer oral route.

FIGURE 8—Serum Levels after Oral Administration of SYNCILLIN (250 mg.) and after Intramuscular Injection of Penicillin G



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

SYNCILLIN has been administered in multiple doses to 437 patients and volunteers. One patient developed itching during therapy, possibly an allergic side effect. Another had a purpuric rash, but no relationship to SYNCILLIN was established. No reactions were observed in 9 patients with a known history of sensitivity to penicillin.

While the above data suggests the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *The usual precautions for oral penicillin therapy should be observed.* Patients with histories of asthma, hay fever, urticaria, or previous penicillin-sensitivity should especially be watched carefully. Since SYNCILLIN is administered orally, it may be expected to be safer than parenteral penicillin.

As Flippin[9] recently stated, "... it is well established that serious allergy to the drug [penicillin] is most likely to occur following parenteral administration, especially after repeated intramuscular injections; the oral route is least likely to initiate severe hypersensitivity reactions. This can be explained partly by the fact that when reactions develop following oral medication, they are usually slow enough to treat symptomatically; thus the progression of the reaction can usually be interrupted.... In view of the relatively high incidence of severe allergy to injectable penicillin, it would seem advisable to employ oral penicillin routinely, except in the control of infections involving the blood stream, endocardium, meninges, etc., in which cases the parenteral route remains the preferred treatment."

SYNCILLIN, like other penicillins, is essentially free of other toxicity. No hematopoietic, hepatic, or renal toxicity was observed in 210 volunteers receiving 1 gm. daily for 2 to 3 weeks.[10]

CLINICAL EFFICACY DEMONSTRATED IN PENICILLIN-SENSITIVE INFECTIONS

Clinical trials conducted by Blau and Kanof,[11] White,[12] Prigot,[13] Robinson,[14] Dube,[15] Ferguson,[16] Rutenburg,[17] Richardson,[18] Bunn,[19] Cronk,[5] Kligman,[10] and Yow [20] demonstrated the efficacy of SYNCILLIN in a variety of streptococcal, staphylococcal, pneumococcal, and gonococcal infections. Conditions treated included respiratory, skin, soft tissue, wound, and chronic urinary tract infections; acute gonorrhea; cellulitis; septicemia; otitis media; gingivitis; and Vincent's angina. In a few patients SYNCILLIN was used for rheumatic fever or gonorrheal prophylaxis.

One hundred seventy-two of one hundred ninety-six patients responded favorably to SYNCILLIN. The failures included 1 patient with pustular dermatoses, 10 elderly patients with chronic urinary tract infections, 1 patient with gonorrhea, 1 patient with a gram-negative infection, and 10 patients with staphylococcal infections. Lack of response of staphylococcal infections was attributed to the presence of resistant organisms or local suppurative foci requiring drainage.

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Relatively few side effects were encountered. One patient experienced moderate itching of the skin which was controlled by an antihistamine. Another reported pruritus ani which did not interfere with therapy. Diarrhea occurred in 4 instances. There was one purpuric rash, but no relationship to SYNCILLIN could be established.

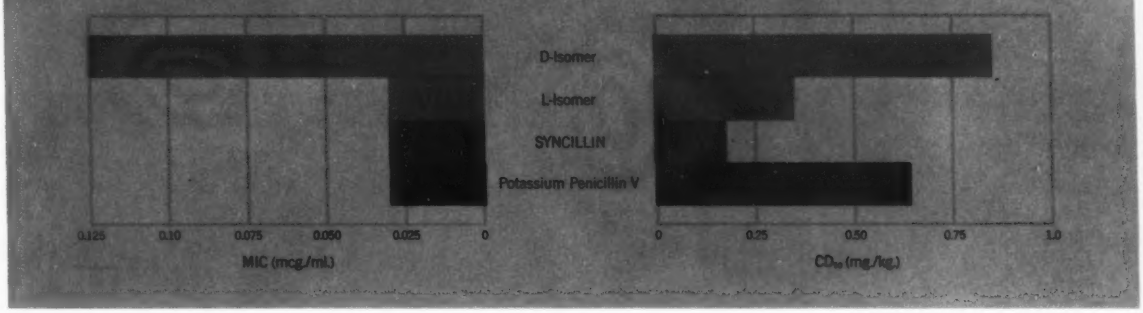
Clinical response usually begins within 24 hours in infections susceptible to SYNCILLIN. Recovery occurs in 4 to 7 days depending upon the severity of the infection. Gonorrheal infections respond very promptly to SYNCILLIN; 500 mg. b.i.d. for two days usually produce bacteriologic cures.

IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

SYNCILLIN is a mixture of isomers. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. Furthermore, the D- and L-isomers have other distinguishing chemical, pharmacological, and microbiological properties. Their *in vivo* and *in vitro* activities differ for many important pathogens. *Against many of the organisms tested, the combination of isomers* (SYNCILLIN) *is much more active than the stronger isomer alone.* This phenomenon of isomeric complementarity is not always demonstrable, for in a few instances SYNCILLIN is slightly less active.

Isomeric complementarity has previously been demonstrated *in vitro* (Figure 4) and *in vivo* (Figure 1). Figure 9 reveals a third form of superiority related to isomeric complementarity. Equal concentrations of SYNCILLIN and penicillin V were required to inhibit this growth of staphylococci *in vitro*. But, *in vivo*, a much smaller amount of SYNCILLIN *(one-third that of penicillin V)* was effective in an experimental infection with the same strain. These observations on complementary action indicated the advantage of producing the mixture of isomers as the medication to be made available for clinical therapy.

FIGURE 9 — Comparison of CD_m and MIC Values Against *Staphylococcus aureus* (var. Smith)



Isomeric complementarity has thus been demonstrated for:

— *certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

— *penicillin-susceptible staphylococci* in vivo *(Figures 1 and 9)*

— *penicillin-resistant staphylococci* in vitro *(Figure 4)*

— *staphylococcal penicillinase antibiotic inactivation (Figure 5)*

SYNCILLIN

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Indications:

SYNCILLIN is recommended in the treatment of infections caused by pneumococci, streptococci, gonococci, corynebacteria, and penicillin-sensitive staphylococci. In addition, SYNCILLIN is effective against certain strains of staphylococci resistant to other penicillins.

SYNCILLIN, like other oral penicillins, is not recommended at the present time in deep-seated or chronic infections, subacute bacterial endocarditis, meningitis, or syphilis.

Dosage:

125 mg. or 250 mg. three times daily, depending on the severity of infection. Larger doses (e.g., 500 mg. t.i.d.) may be used for more severe infections. SYNCILLIN may be administered without regard to meals.

Beta hemolytic streptococcal infections should be treated with SYNCILLIN for at least ten days.

Precautions:

While present data suggest the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *Therefore the usual precautions with oral penicillin therapy must be observed.* Patients with histories of asthma, hay fever, urticaria, or previous reactions to penicillin should be watched with special care.

Diarrhea has been reported occasionally following heavy dosage. If this occurs, the interval between dosages should be lengthened.

If superinfection occurs during therapy, appropriate measures should be taken.

Since some strains of staphylococci are resistant to SYNCILLIN as well as to other penicillins, cultures and sensitivity tests should be performed where indicated by clinical judgment. As is true with all antibiotics, clinical response does not always correlate with laboratory bacterial sensitivity reports.

Supply:

125 and 250 mg. tablets, bottles of 25 and 100. 125 mg. powder for oral solution, 60 ml. vials.

References: 1. Lein, J.: Microbiology report to Bristol Laboratories Inc. 2. Wright, W. W.: Microbiology report to Bristol Laboratories Inc. 3. White, A. C.: Microbiology report to Bristol Laboratories Inc. 4. Dubos, R. J.: Bacterial and Mycotic Infections of Man, 3rd edition, Philadelphia, J. B. Lippincott Co., p. 690. 5. Cronk, G. A.: Clinical report to Bristol Laboratories Inc. 6. Wright, W. W.: Clinical report to Bristol Laboratories Inc. 7. Kass, E. H.: Am. J. Med. *18*:764 (May) 1955. 8a. White, A. C.; Couch, R. A.; Foster, F.; Calloway, J.; Hunter, W., and Knight, V.: in Welch, H. and Marti-Ibañez, F.: Antibiotics Annual — 1955-1956, Medical Encyclopedia, Inc., New York, 1956, p. 490. b. Data on file — at Bristol Laboratories. 9. Flippin, H. F.: Pennsylvania M. J. *62*:864 (June) 1959. 10. Kligman, A.: Clinical report to Bristol Laboratories Inc. 11. Blau, S., and Kanof, N.: Clinical report to Bristol Laboratories Inc. 12. White, A. C.: Clinical report to Bristol Laboratories Inc. 13. Prigot, A.: Clinical report to Bristol Laboratories Inc. 14. Robinson, C.: Clinical report to Bristol Laboratories Inc. 15. Dube, A. H.: Clinical report to Bristol Laboratories Inc. 16. Ferguson, B.: Clinical report to Bristol Laboratories Inc. 17. Rutenburg, A. M.: Clinical report to Bristol Laboratories Inc. 18. Richardson, J. H.: Clinical report to Bristol Laboratories Inc. 19. Bunn, P. A.: Clinical report to Bristol Laboratories Inc. 20. Yow, E. M.: Clinical report to Bristol Laboratories Inc.

BRISTOL

major therapeutic advantages accompany molecular asymmetry

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ALTAFUR in antibiotic-resistant staphylococcal infections

ALTAFUR proved superior to any other single agent against staphylococcal infections encountered in the pediatric section of a general hospital. Introduced during an epidemic of severe staphylococcal pneumonia and bronchiolitis in younger children, ALTAFUR was employed in treating a total of 59 infants or juvenile patients, most of whom had upper or lower respiratory tract involvement. Almost all had been given antibiotics without effect; 34 were judged severely or critically ill. Cures were obtained in 54 of these patients after a 3 to 10 day course of ALTAFUR. There was only one failure (results were inconclusive in the remaining four cases). Mixed infections with Pneumococcus or Streptococcus sp. also responded readily.

ALTAFUR was administered orally in varying dosage: the optimal dose is believed to be about 22 mg./Kg. daily.

Side effects were minimal in these patients, being limited to gastric intolerance in a few cases, usually controllable by giving the drug with or after meals. Laboratory studies performed before and after ALTAFUR treatment revealed no adverse influence on renal, hepatic or hematopoietic function, nor other signs of toxicity.

In vitro, staphylococci isolated in this series proved uniformly susceptible to ALTAFUR, whereas many strains were resistant to a variety of antibotics. With ALTAFUR as with all nitrofurans, the lack of development of significant bacterial resistance is considered a major advantage over other antimicrobials.

Lysaught, J. N., and Cleaver, W.: Paper presented at the Symposium on Antibacterial Therapy, Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959 (published Nov., 1959)

bright new star

in the antibacterial firmament

ALTAFUR™

brand of furaltadone

the first nitrofuran effective orally in systemic bacterial infections

- Antimicrobial range encompasses the majority of common infections seen in everyday office practice and in the hospital
- Decisive bactericidal action against staphylococci, streptococci, pneumococci, coliforms
- Sensitivity of staphylococci in vitro (including antibiotic-resistant strains) has approached 100%
- Development of significant bacterial resistance has not been encountered
- Low order of side effects
- Does not destroy normal intestinal flora nor encourage monilial overgrowth (little or no fecal excretion)

Tablets of 50 mg. (pediatric) and 250 mg. (adult)
Average adult dose: 250 mg. four times a day, with food or milk
Pediatric dosage: 22-25 mg./Kg. (10-11.5 mg./lb. body weight daily in 4 divided doses

CAUTION: The ingestion of alcohol in any form, medicinal or beverage, should be avoided during Altafur therapy.

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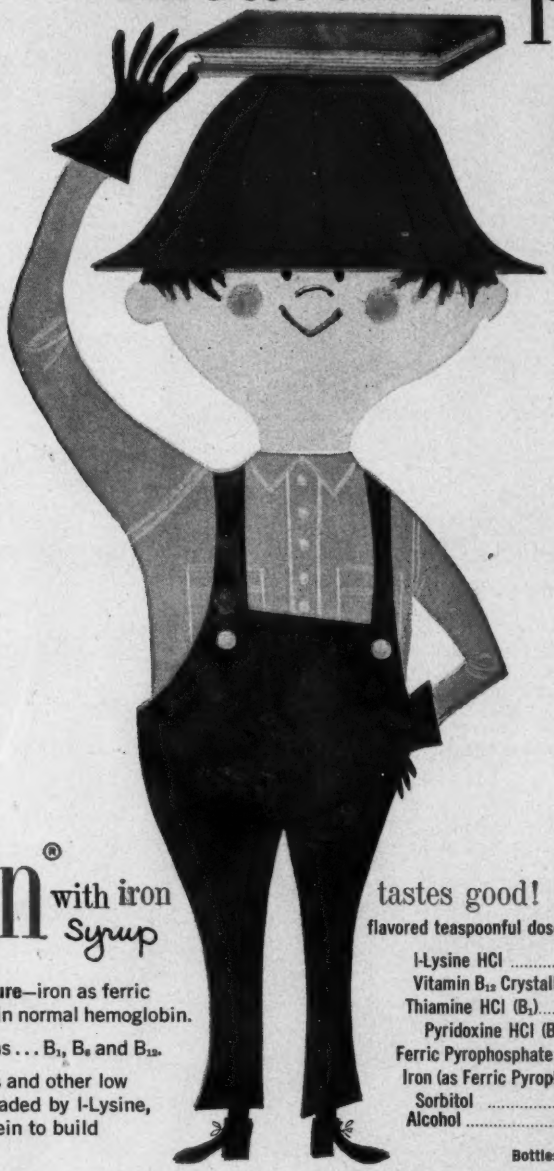
EATON LABORATORIES, NORWICH, NEW YORK

make them measure up



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upgrade low-grade protein—cereals and other low protein favorites of children, upgraded by l-Lysine, work with meat and other top protein to build stronger bodies.

tastes good! Each daily cherry-flavored teaspoonful dose (5 cc.) contains:

l-Lysine HCl	300 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine HCl (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Ferric Pyrophosphate (Soluble)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Sorbitol	3.5 Gm.
Alcohol	0.75%

Bottles of 4 and 16 fl. oz.

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The need for PROTECTION is obvious!

Fires — tornados — hurricanes — make newspaper headlines and protection against financial loss from these sources is commonly considered necessary. A major accident or illness can be equally disastrous to a family's finances.

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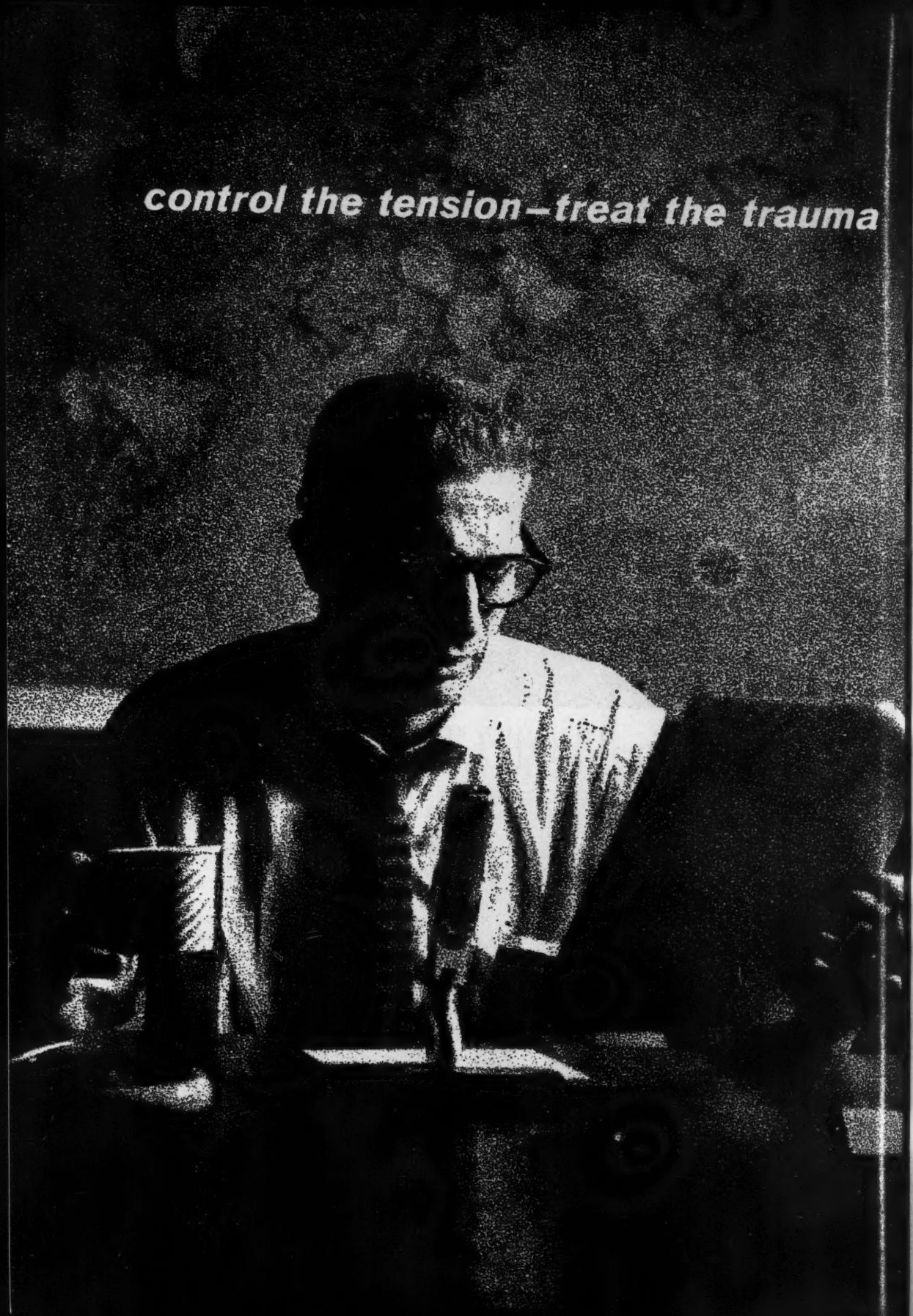
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...Pathibamate® 400 200

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greater flexibility in the control of tension, hypermotility and excessive secretion in gastrointestinal dysfunctions

PATHIBAMATE combines two highly effective and well-tolerated therapeutic agents:

meprobamate (400 mg. or 200 mg.) widely accepted tranquilizer and . . .
PATHILON (25 mg.)—anticholinergic noted for its peripheral, atropine-like action, with few side effects.

The clinical advantages of PATHIBAMATE have been confirmed by nearly two years' experience in the treatment of duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms and gastric hypermotility.

Because of individual variation in the intensity of stimuli in gastrointestinal disorders, adequate dosage for optimum control may be expected to vary as well. The dosage strengths of PATHIBAMATE-400 and PATHIBAMATE-200 facilitate individualization of treatment in respect to both the degree of tension and associated G.I. sequelae, as well as the response of different patients to the component drugs.

Supplied: PATHIBAMATE-400—Each tablet (yellow, 1/2-scored) contains meprobamate, 400 mg.; PATHILON tridihexethyl chloride, 25 mg.
PATHIBAMATE-200—Each tablet (yellow, coated) contains meprobamate, 200 mg.; PATHILON tridihexethyl chloride, 25 mg.

Administration and Dosage: PATHIBAMATE-400—1 tablet three times a day at mealtime and 2 tablets at bedtime.
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Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

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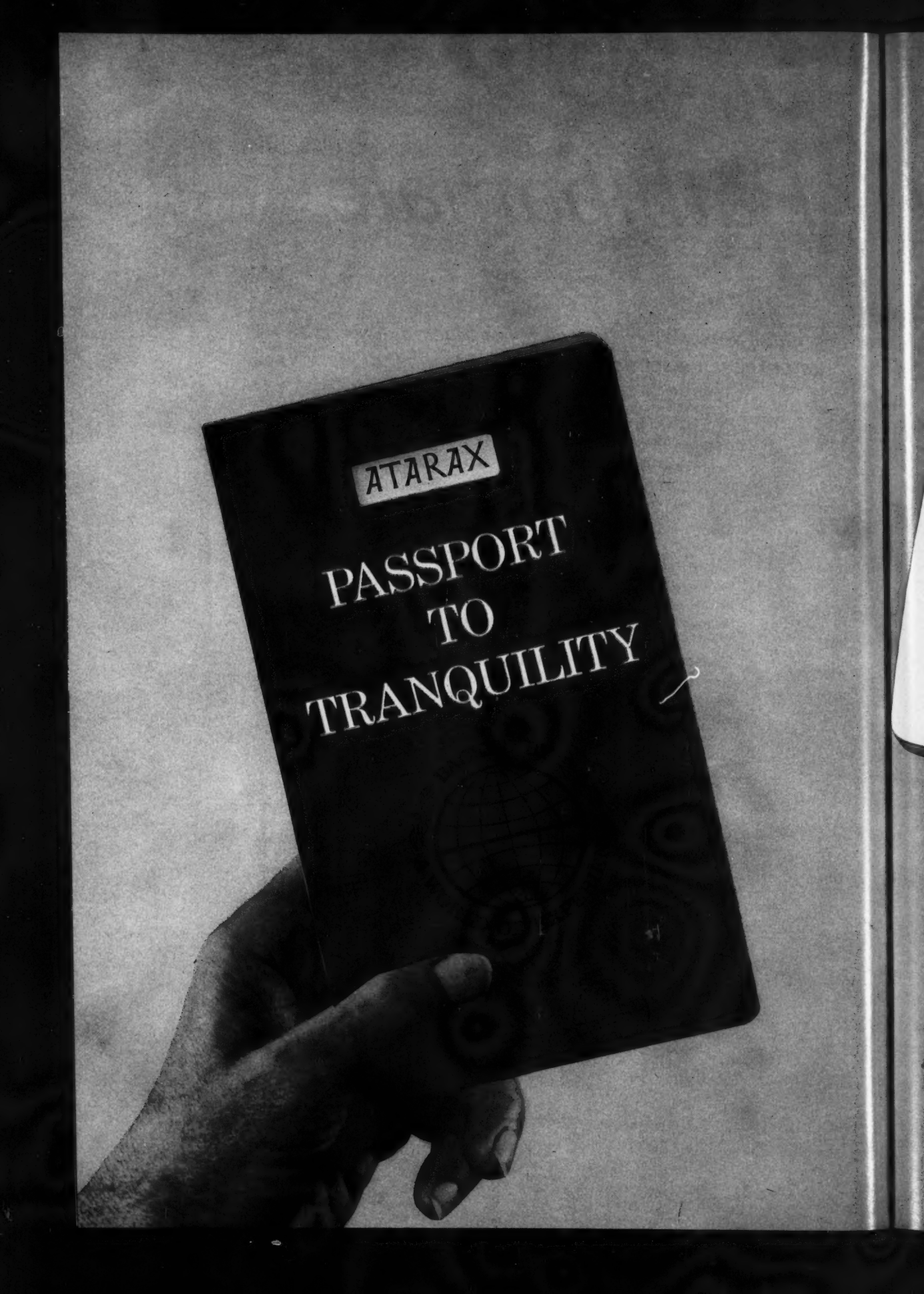
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TO
TRANQUILITY

Passport

☞ **a universal record of effectiveness**

In anxiety, tension and agitation, ATARAX "... produced a more favorable state of calm and tranquility than any drug previously used."[1]

☞ **widest latitude of safety and flexibility**

No serious adverse reaction ever documented – five dosage forms and sizes

☞ **chemically distinct among tranquilizers**

Not a phenothiazine or a meprobamate

☞ **added frontiers of usefulness**

These unique benefits in specific indications

ANTIHISTAMINIC
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BACKED BY A WORLD OF EXPERIENCE

Dosage: ADULTS, one 25 mg. tablet, or one tbsp. Syrup q.i.d. CHILDREN – 3-6 years, one 10 mg. tablet or one tsp. Syrup t.i.d.; over 6 years, two 10 mg. tablets or two tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Farah, L.: Internat. Rec. Med. *169*:379 (June) 1956. 2. Smigel, J. O., et al.: J. Am. Geriatrics Soc. *7*:61 (Jan.) 1959. 3. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 4. Eisenberg, B. C.: J.A.M.A. *169*:14 (Jan. 3) 1959. 5. Maryssael, L.: Bruxelles-méd. *38*:141 (Jan. 26) 1958. 6. Pfleger, R.: Med. Klin. *53*:1030 (June 5) 1958. 7. Over 200 laboratory and clinical papers from 14 countries.

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a logical combination in appetite control

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meprobamate with dextro-amphetamine sulfate LEDERLE

meprobamate eases
tensions of dieting

d-amphetamine
depresses appetite
and elevates mood

...without
overstimulation

...without
insomnia

...without
barbiturate hangover

Each coated tablet (pink) contains:
d-amphetamine sulfate .... 5 mg.
meprobamate ..... 400 mg.
Dosage: One tablet taken one-half to one hour before each meal.

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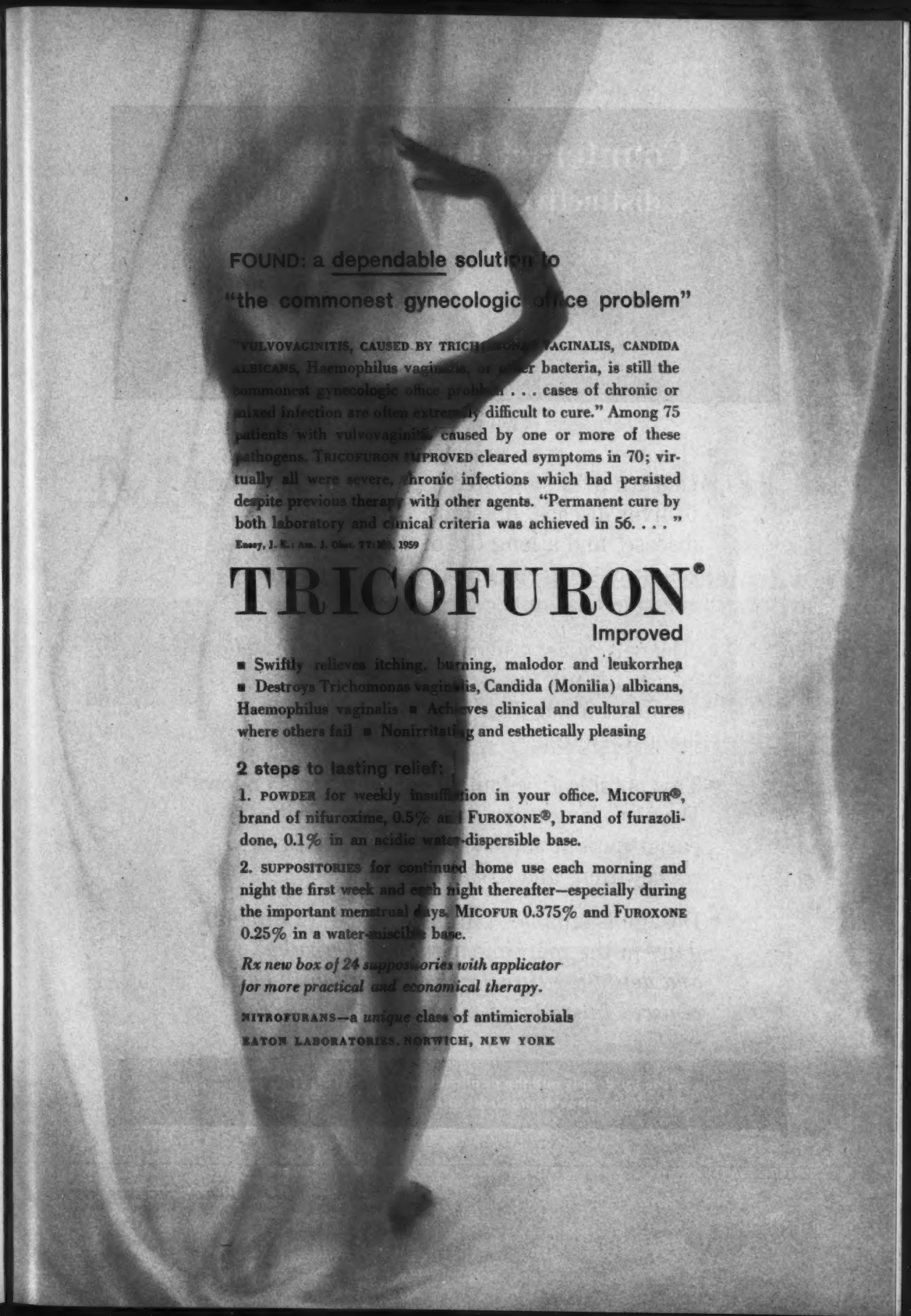

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"the commonest gynecologic office problem"

"VULVOVAGINITIS, CAUSED BY TRICHOMONAS VAGINALIS, CANDIDA ALBICANS, Haemophilus vaginalis, or other bacteria, is still the commonest gynecologic office problem . . . cases of chronic or mixed infection are often extremely difficult to cure." Among 75 patients with vulvovaginitis caused by one or more of these pathogens, TRICOFURON IMPROVED cleared symptoms in 70; virtually all were severe, chronic infections which had persisted despite previous therapy with other agents. "Permanent cure by both laboratory and clinical criteria was achieved in 56. . . ."

Essey, J. E.: Am. J. Obst. 77:[illegible], 1959

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■ Swiftly relieves itching, burning, malodor and leukorrhea ■ Destroys Trichomonas vaginalis, Candida (Monilia) albicans, Haemophilus vaginalis ■ Achieves clinical and cultural cures where others fail ■ Nonirritating and esthetically pleasing

2 steps to lasting relief:

1. POWDER for weekly insufflation in your office. MICOFUR®, brand of nifuroxime, 0.5% and FUROXONE®, brand of furazolidone, 0.1% in an acidic water-dispersible base.

2. SUPPOSITORIES for continued home use each morning and night the first week and each night thereafter—especially during the important menstrual days. MICOFUR 0.375% and FUROXONE 0.25% in a water-miscible base.

Rx new box of 24 suppositories with applicator for more practical and economical therapy.

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- 'Deaner' may be prescribed with little or no concern over side effects even in the presence of liver disease, diabetes, cardiovascular disease, and a long list of other chronic conditions, except grand mal epilepsy (only contraindication).
- 'Deaner' *is not a monoamine oxidase inhibitor;* hence it is not necessary to monitor its administration with repeated, expensive laboratory tests.
- This notable freedom from side effects endows Deaner's long-term administration with easier patient supervision, better patient cooperation, and greater safety.
- Dosage is simple—initially, 50 mg. (2 tablets) daily in the morning. *Gradually, apathy and defeat are transformed into affability and renewed interest and vigor.*

Write for details and the applicability of 'Deaner' in behavior problems of children

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FOR SUSTAINED TRANQUILIZATION

MILTOWN® (*meprobamate*) now available in 400 mg. continuous release capsules as

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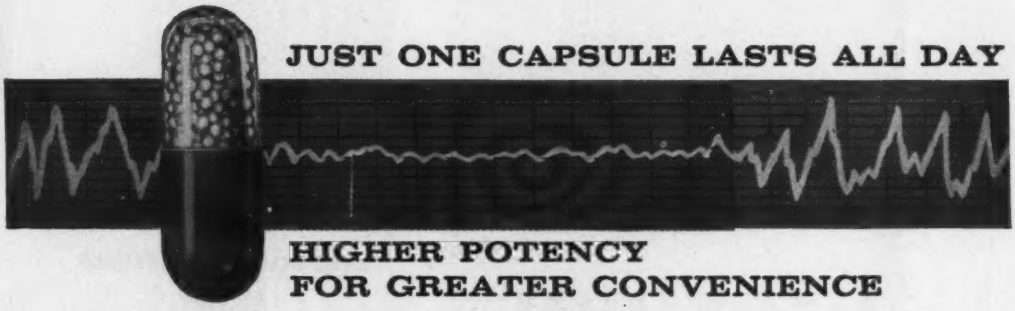

JUST ONE CAPSULE LASTS ALL DAY

HIGHER POTENCY FOR GREATER CONVENIENCE

- relieves *both* mental and muscular tension without causing depression
- does not impair mental efficiency, motor control, or normal behavior

Usual dosage: One capsule at breakfast, one capsule with evening meal

Available: *Meprospan-400*, each blue capsule contains 400 mg. Miltown (meprobamate)
Meprospan-200, each yellow capsule contains 200 mg. Miltown (meprobamate)

Both potencies in bottles of 30.

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meprobamate *plus* d-amphetamine

...depresses appetite...elevates mood...eases tensions of dieting...*without* overstimulation, insomnia, or barbiturate hangover.

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Each coated tablet (pink) contains: meprobamate, 400 mg.; d-amphetamine sulfate, 5 mg. Dosage: One tablet one-half to one hour before each meal.

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ON LETTERS AND PACKAGES

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the **Elixir**

complete attack on

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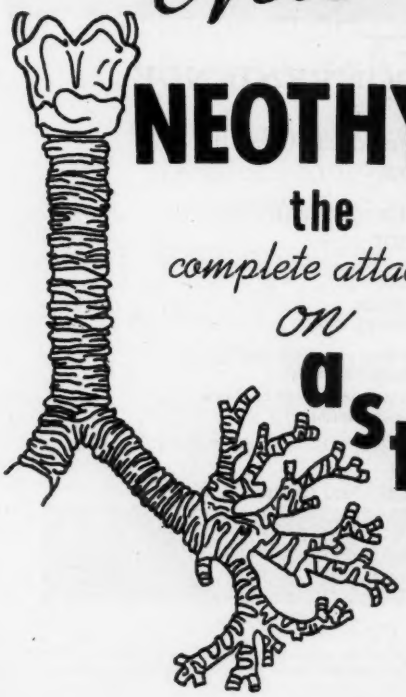

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Liquefaction of Tenacious Mucous

Each 5cc Contains:

Butabarbital Sodium	16 Mg.	(¼ Gr.)
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Calcium Iodide	81 Mg.	(1¼ Gr.)
Ephedrine Hcl	8 Mg.	(⅛ Gr.)

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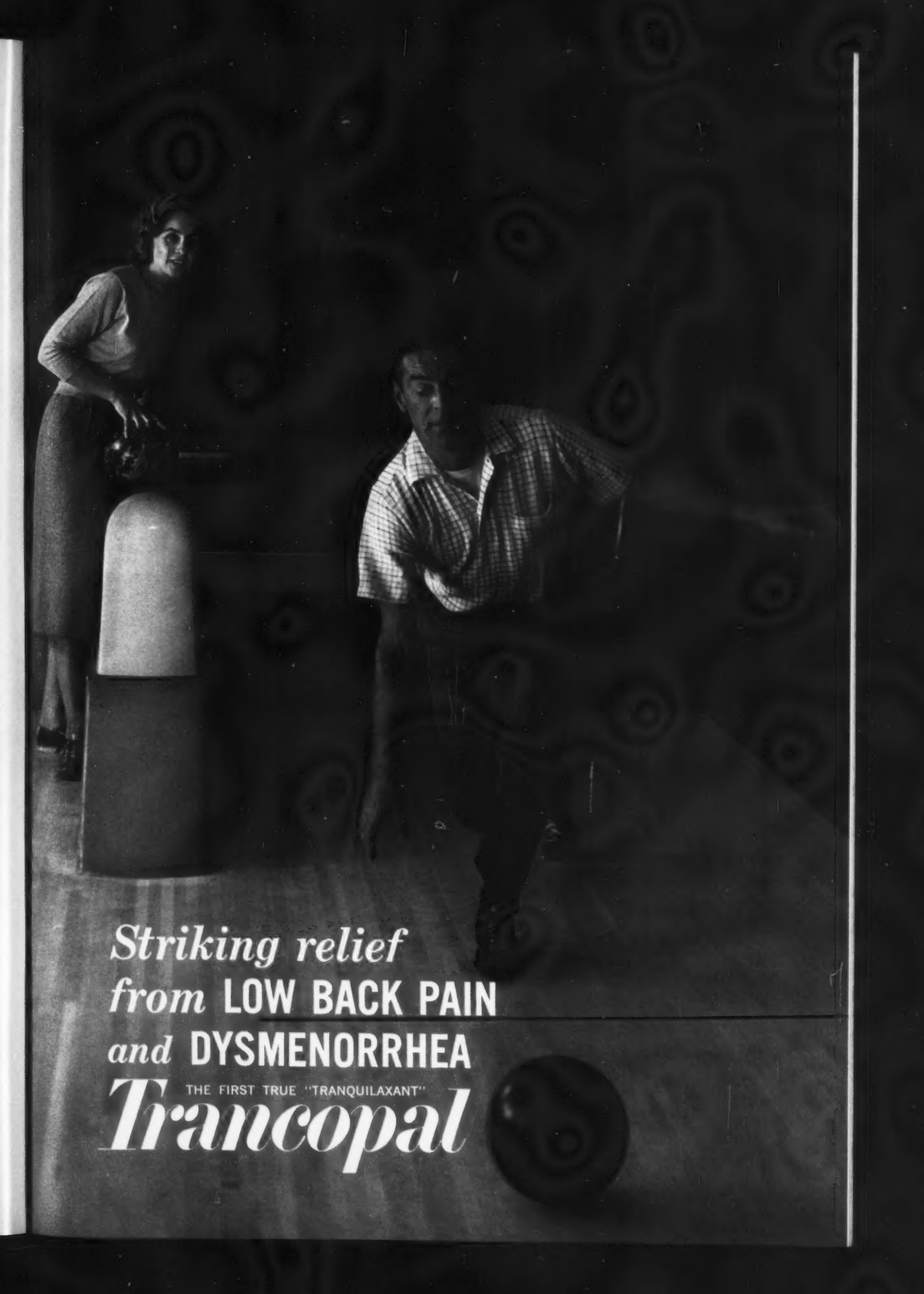

Striking relief
from LOW BACK PAIN
and DYSMENORRHEA
THE FIRST TRUE "TRANQUILAXANT"
Trancopal

Here is what you can expect when you prescribe

for dysmenorrhea

and premenstrual tension

Case Profile*

A 28-year-old married woman, a secretary in a booking agency, complained of severe and consistent pain and cramps in the abdomen during her menstrual periods. Psychologically, she described the first two days as "climbing the walls." Menarche occurred at age 13. She has a regular twenty-eight day menstrual cycle and a four day menstrual period.

Trancopal was given in a dose of 100 mg. four times a day for the first two days of the four day period. In addition to the relief of the dysmenorrhea she also noticed disappearance of a "bloated feeling" that had previously annoyed her. She has now been treated with Trancopal for one and one-half years with excellent results. Other medication, such as codeine or aspirin with codeine, had relieved the pain, but the patient had had to stay home. Because her father is a physician, many commercial preparations had been tried prior to Trancopal, but no success had been achieved.

Before taking Trancopal this patient missed one day of work every month. For the past year and a half she has not missed a day because of dysmenorrhea.

THE FIRST TRUE "TRANQUILAXANT"

Trancopal®

for low back pain

Case Profile*

A 42-year-old truck driver and mover injured his back while moving a piano. The pain radiated from the sacral region down to the region of the Achilles tendon on the right side. X-rays for ruptured disc revealed nothing pertinent. The day of the injury he was given Trancopal immediately after the physical examination. Although 100 to 200 mg. three times a day were prescribed, the patient on his own responsibility increased the dosage of Trancopal to 400 mg. three times a day. This dosage was continued for three days and then gradually reduced over a ten day period. During this time, the patient continued to drive his truck. The muscle spasm was completely controlled and no apparent side effects were noted.

For the past six months, the patient has continued to take Trancopal 100 to 200 mg. as needed for muscle spasm, particularly during strenuous days.

**Clinical Reports on file at the Department of Medical Research, Winthrop Laboratories.*

Turn page for complete listings of Indications and Dosage.

THE FIRST TRUE "TRANQUILAXANT"

Trancopal

potent MUSCLE RELAXANT

effective TRANQUILIZER

- In musculoskeletal disorders, effective in 91 per cent of patients.[1]
- In anxiety and tension states, effective in 89 per cent of patients.[1]
- Low incidence of side effects (2.3 per cent of patients). Blood pressure, pulse rate, respiration and digestive processes are unaffected by therapeutic dosage. It does not affect the hematopoietic system or liver and kidney function.
- No gastric irritation. Can be taken before meals.
- No clouding of consciousness, no euphoria or depression.

Indications [1-6]

Musculoskeletal:

Low back pain (lumbago, etc.)
Neck pain (torticollis)
Bursitis
Rheumatoid arthritis
Osteoarthritis
Disc syndrome
Fibrositis
Ankle sprain, tennis elbow
Myositis
Postoperative muscle spasm

Psychogenic:

Anxiety and tension states
Dysmenorrhea
Premenstrual tension
Asthma
Angina pectoris
Alcoholism

Now available in two strengths:

Trancopal Caplets®,
100 mg. (peach colored, scored), bottles of 100.

NEW STRENGTH ▶

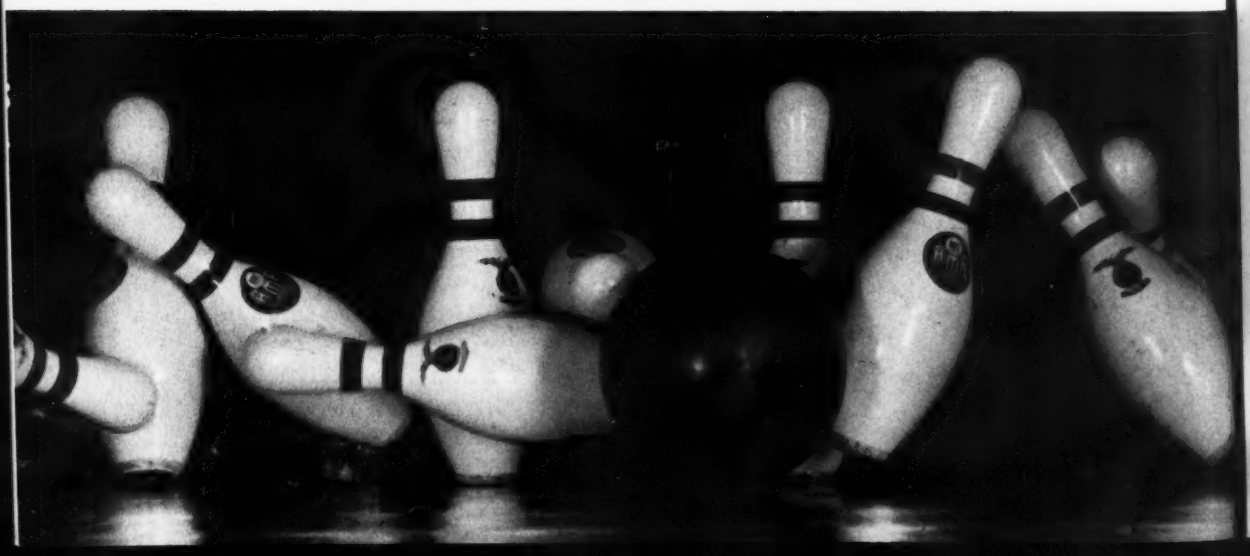
Trancopal Caplets,
200 mg. (green colored, scored), bottles of 100.

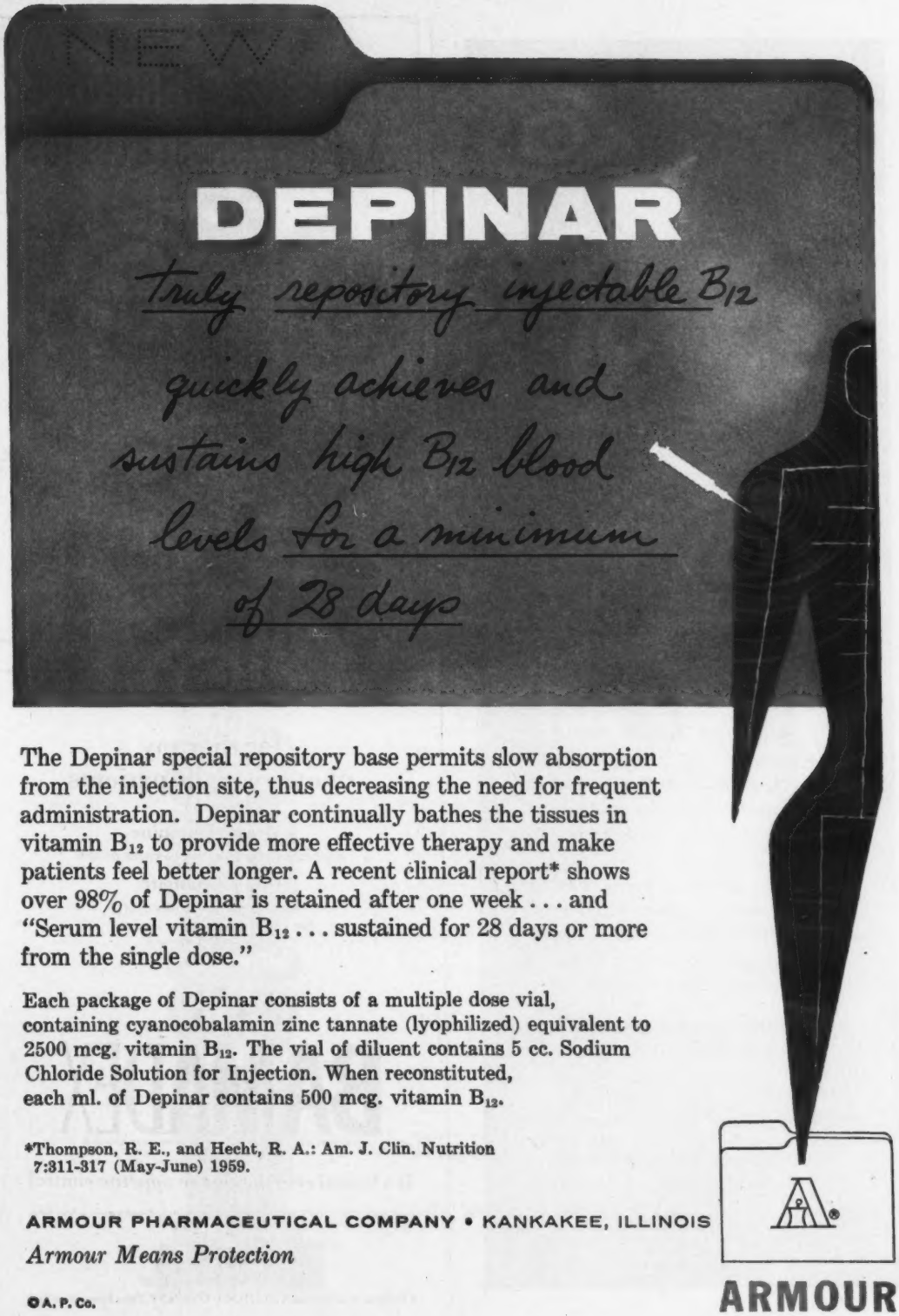
Dosage: Adults, 100 or 200 mg. orally three or four times daily. Relief of symptoms occurs in from fifteen to thirty minutes and lasts from four to six hours.

Winthrop LABORATORIES
New York 18, N. Y.

References: 1. Collective Study, Department of Medical Research, Winthrop Laboratories. 2. Lichtman, A. L.: New developments in muscle relaxant therapy, *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958. 3. Lichtman, A. L.: Relief of muscle spasm with a new central muscle relaxant, chlormezanone (Trancopal), Scientific Exhibit, Meeting of the International College of Surgeons, Miami Beach, Fla., Jan. 4-7, 1959. 4. Ganz, S. E.: Clinical evaluation of a new muscle relaxant (chlormethazanone), *J. Indiana M. A.* 52:1134, July, 1959. 5. Mullin, W. G., and Epifano, Leonard: Chlormezanone, a tranquilizing agent with potent skeletal muscle relaxant properties, *Am. Pract. Digest Treat.* 10:1743, Oct., 1959. 6. Shanaphy, J. F.: Chlormezanone (Trancopal) in the treatment of dysmenorrhea; a preliminary report, *Current Therap. Res.* 1:59, Oct., 1959.

Trancopal (brand of chlormezanone) and Caplets, trademarks reg. U.S. Pat. Off. 1408M Printed in U.S.A.





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*Thompson, R. E., and Hecht, R. A.: Am. J. Clin. Nutrition 7:311-317 (May-June) 1959.

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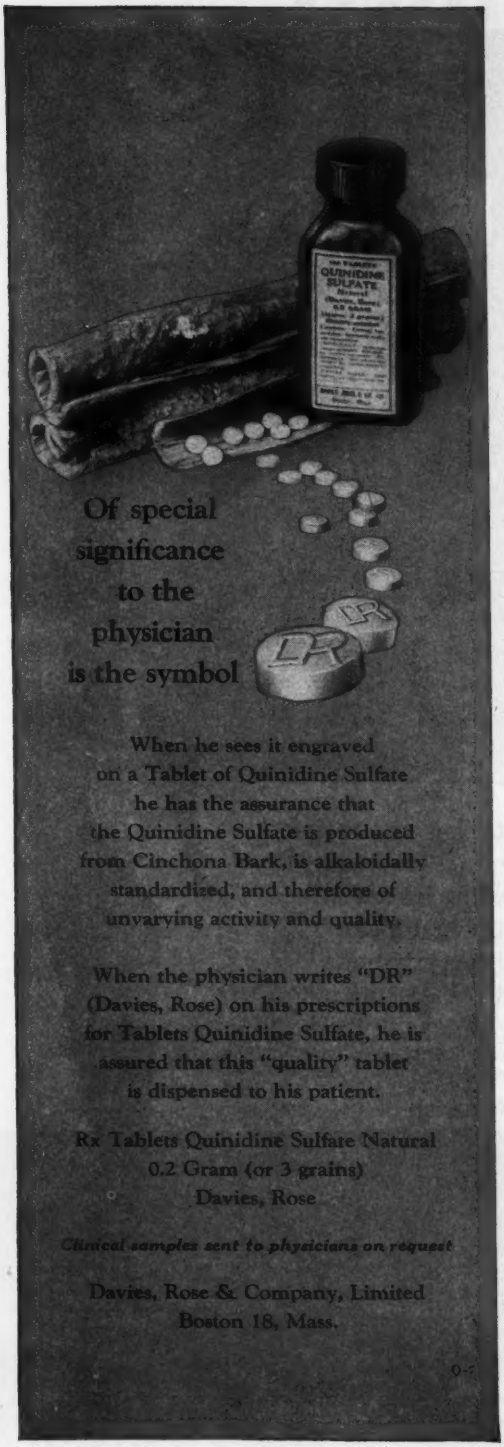
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• **d-amphetamine**
depresses appetite and elevates mood
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eases tensions of dieting
(yet without overstimulation, insomnia or barbiturate hangover)

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Dosage: One tablet one-half to one hour before each meal.

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the disease of many masks

Doctor, do you recognize this patient? She complains of flatulence, constipation with alternating periods of diarrhea, and colicky pains in the lower right quadrant. At other times she is troubled by anorexia, lassitude, dull headache, muscle pains and backache. Or she may have only one or two of these symptoms.

In these puzzling cases, serious consideration should be given to intestinal amebiasis—the disease of many masks. Clinicians say it is "one of the most widespread and serious protozoan diseases of man," yet "there is no parasite more often misdiagnosed than is *E. histolytica*." Conservative estimates place the incidence at 10% of the United States population as a whole, and 16% in southern states.

Now Glarubin, a relatively non-toxic amebicide, simplifies the treatment of suspected cases of intestinal amebiasis. Glarubin, a crystalline glycoside from the fruit of *Simarouba glauca*, is a specific amebicidal agent with minimal side effects. It contains no arsenic, bismuth or iodine.

Glarubin is administered orally in tablet form and does not require strict medical supervision or hospitalization. Extensive clinical trials prove it highly effective in intestinal amebiasis, and virtually free of toxicity.

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new Glarubin

TABLETS

specific for intestinal amebiasis

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HOW PREVALENT ARE MULTIPLE GALLBLADDER ANOMALIES?

One hundred and twenty-two cases of *vesica fellea divisa* (bilobed gallbladder) and *vesica fellea duplex* (double gallbladder with 2 cystic ducts) are reported in the literature. A unique case of *vesica fellea triplex* has recently been described.

Source: Skilboe, B.: Am. J. Clin. Path. *30*:252, 1958.

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free-flowing bile
plus reliable spasmolysis

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"...DECHOLIN/Belladonna in a dosage of one tablet t.i.d. for a period of two to three months may prove helpful in relieving postoperative symptoms, aiding the digestion, and facilitating elimination."[2]

(1) Beckman, H.: Drugs: Their Nature, Action and Use, Philadelphia, W. B. Saunders Company, 1958, p. 425.
(2) Biliary Tract Diseases, M. Times *85*:1081, 1957.

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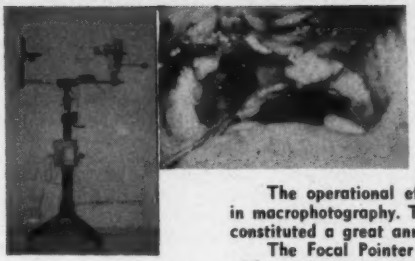

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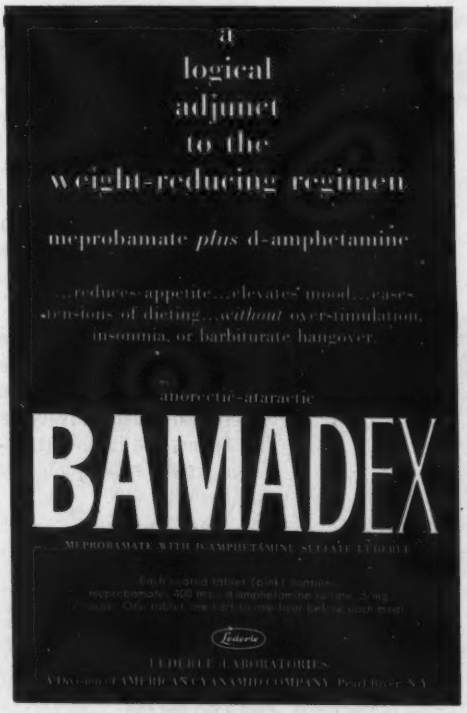

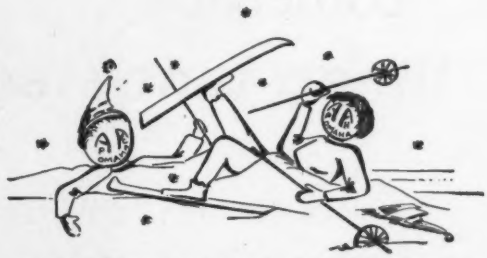

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